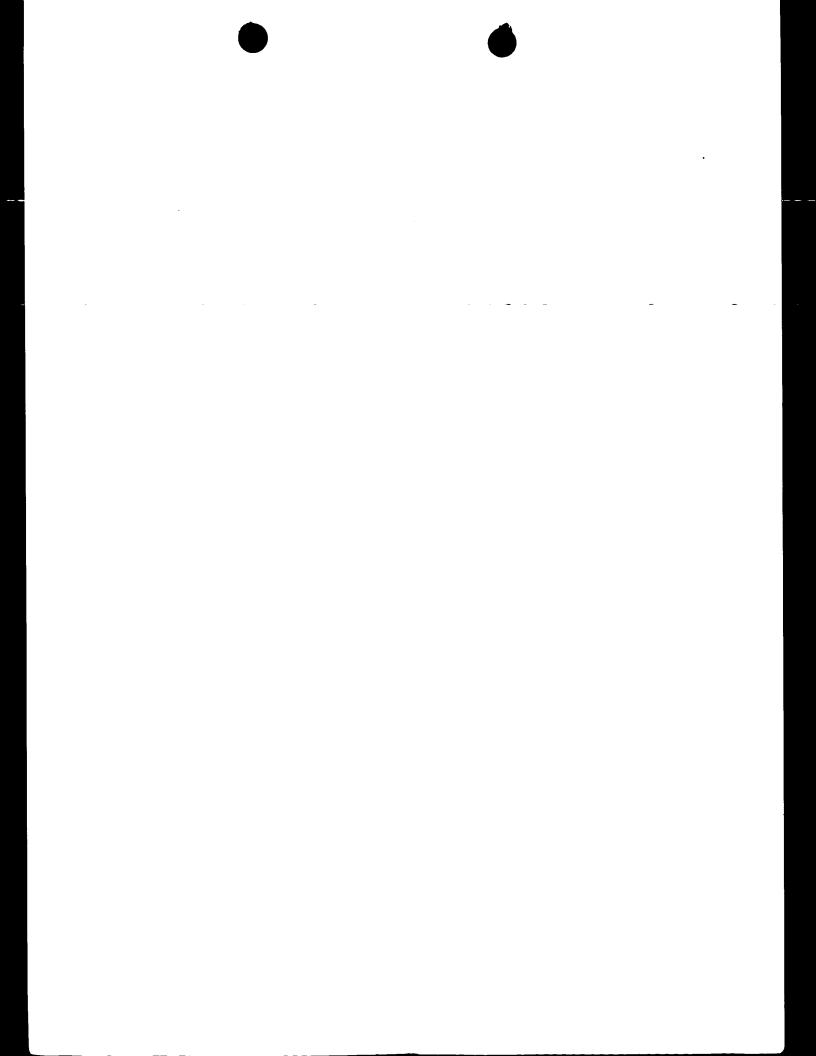
(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference X-11600	FOR FURTHER see Notification of (Form PCT/ISA/2	of Transmittal of International Search Report 220) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/US 00/06707	09/05/2000	11/05/1999
Applicant ELI LILLY AND COMPANY		
This International Search Report has bee according to Article 18. A copy is being tr	n prepared by this International Searching Aut ansmitted to the International Bureau.	hority and is transmitted to the applicant
	of a total of5sheets. a copy of each prior art document cited in this	report.
1. Basis of the report		
a. With regard to the language, the language in which it was filed, un	international search was carried out on the bar less otherwise indicated under this item.	sis of the international application in the
the international search w Authority (Rule 23.1(b)).	as carried out on the basis of a translation of t	he international application furnished to this
b. With regard to any nucleotide an was carried out on the basis of the	d/or amino acid sequence disclosed in the inesequence listing:	ternational application, the international search
l. —	onal application in written form.	
filed together with the inte	mational application in computer readable for	n.
X furnished subsequently to	this Authority in written form.	
X furnished subsequently to	this Authority in computer readble form.	
the statement that the sub international application a	sequently furnished written sequence listing dissing dissipports been furnished.	oes not go beyond the disclosure in the
X the statement that the info furnished	ormation recorded in computer readable form is	s identical to the written sequence listing has been
2. X Certain claims were fou	nd unsearchable (See Box I).	
3. Unity of invention is lac	king (see Box II).	
4. With regard to the title,		
the text is approved as su	bmitted by the applicant.	
the text has been establis	hed by this Authority to read as follows:	
5. With regard to the abstract,		
the text is approved as su the text has been establis within one month from the	bmitted by the applicant. hed, according to Rule 38.2(b), by this Authorit date of mailing of this international search rep	y as it appears in Box III. The applicant may, ort, submit comments to this Authority.
6. The figure of the drawings to be publi		
as suggested by the applie		None of the figures.
because the applicant faile		
	characterizes the invention.	



International Application No. PCT/US 00 \(06707 \)

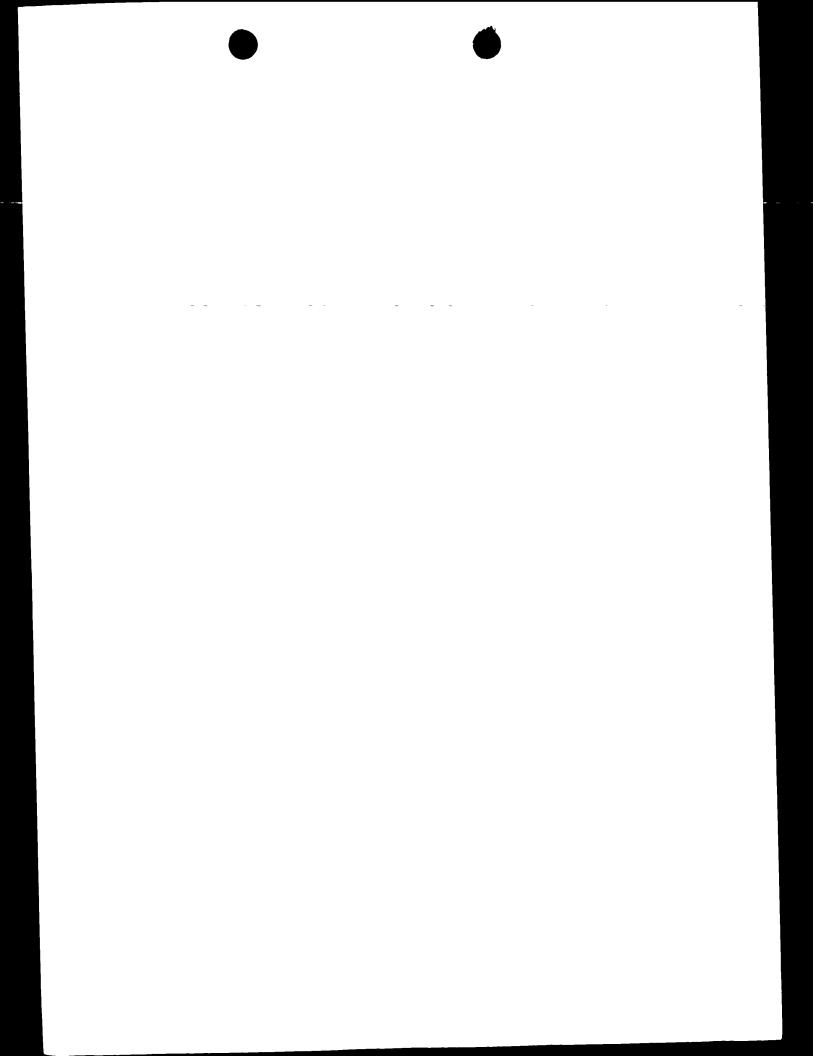
FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 21,22

Claims 21 and 22 refer to an antagonist/inhibitor of the polypeptide without giving a true technical characterization. Moreover, no such compunds are defined in the application. In consequence, the scope of said claims is ambigous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 6 PCT). No search could be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the result to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



PCT Application No 00/06707

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K14/47 C12N15/57 A61P25/28

C12N9/64

C12N5/10

C12N5/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\begin{array}{ll} \mbox{Minimum documentation searched (classification system followed by classification symbols)} \\ IPC 7 C12N C07K A61P \end{array}$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

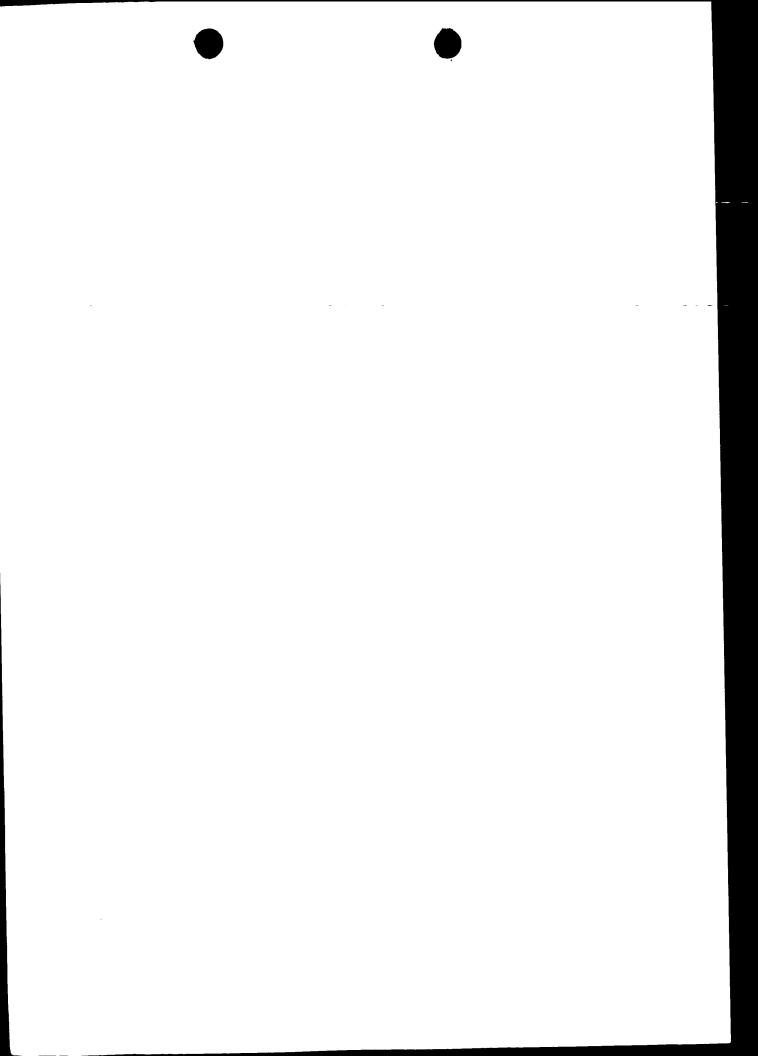
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

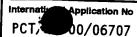
STRAND, EMBL, GENSEQ, EPO-Internal

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE GENEMBL 'Online! 6 June 1996 (1996-06-06) HILLIER ET AL.: "yx480g8.rl soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:265022 5' similar to contains Alu repetitive element" XP002148339 Accesion number N30496	1-16
x	WO 96 40885 A (MCCONLOGUE LISA C ;KEIM PAMELA S (US); SINHA SUKANTO (US); TAN HUA) 19 December 1996 (1996-12-19) page 22, line 20 -page 23, line 2 page 41, line 20 -page 48, line 34 claims 23-41; table 3	17

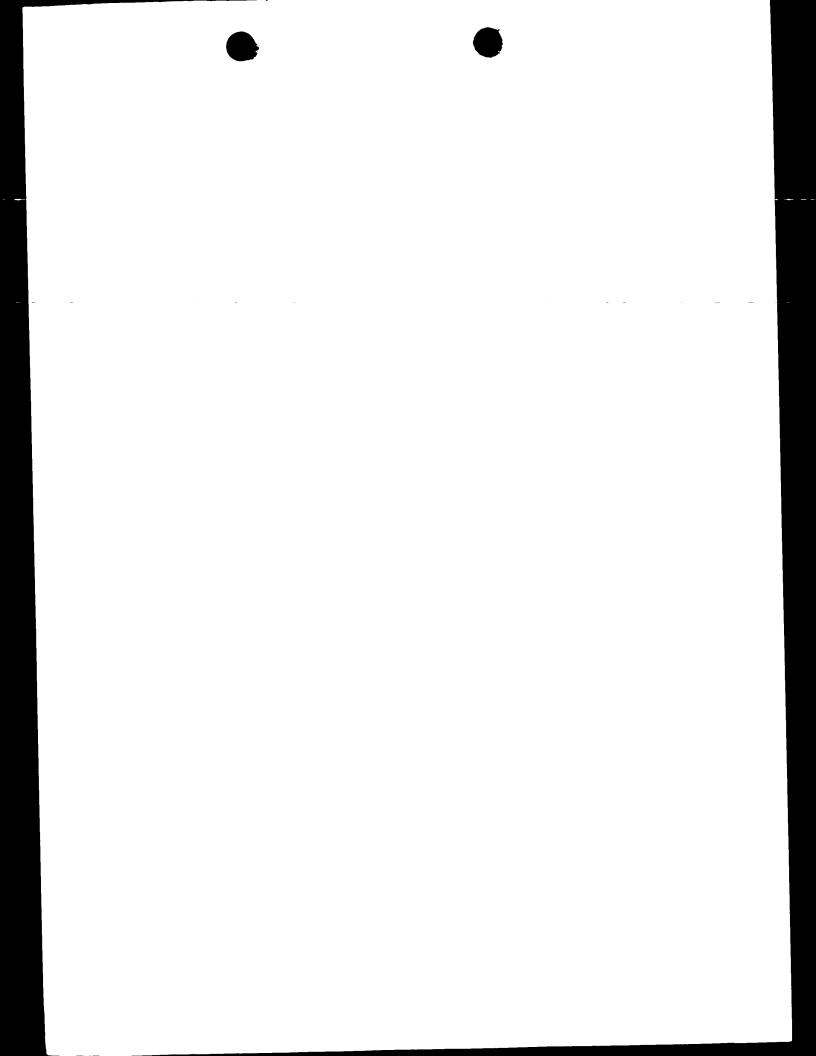
X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
Special categories of cited documents :	
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	 "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
4 October 2000	17/10/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL – 2280 HV Rijswijk	Authorized officer
Tel. (+31–70) 340–2040, Tx. 31 651 epo ni, Fax: (+31–70) 340–3016	ALCONADA RODRIG, A
YM PCT/ICA/D10 (assessed at all 1)	

Form PCT/ISA/210 (second sheet) (July 1992)





PCT 00/06707
Relevant to claim No.
nelevant to claim No.
19
1-16
1-16

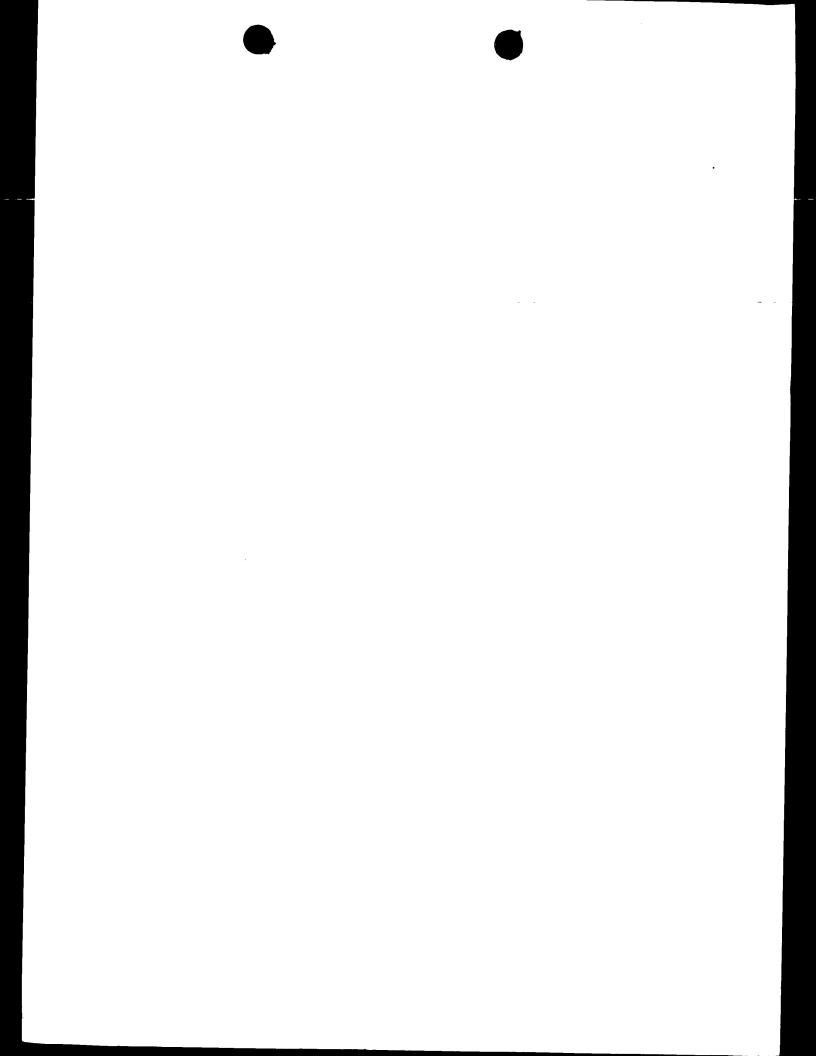


Informatio

atent family members

Internation Application No
PCT/ 00/06707

Patent document cited in search report		Publication date		atent family member(s)	Publication date	
WO 9640885	A	19-12-1996	US AU EP JP US	5744346 A 6383396 A 0871720 A 11507538 T 5942400 A	28-04-1998 30-12-1996 21-10-1998 06-07-1999 24-08-1999	
EP 0653154	A	17-05-1995	JP CA US	7132033 A 2135595 A 6037521 A	23-05-1995 13-05-1995 14-03-2000	
WO 9946281	A	16-09-1999	AU AU WO AU EP WO AU EP WO	3072199 A 3075099 A 9947677 A 1532499 A 1032667 A 9927098 A 3757099 A 9954467 A 1070399 A 1025227 A 9920756 A	27-09-1999 11-10-1999 23-09-1999 15-06-1999 06-09-2000 03-06-1999 08-11-1999 28-10-1999 10-05-1999 09-08-2000 29-04-1999	



PATENT COOPERATION TRE by fax and post From the INTERNATIONAL PRELIMINARY, EXAMINING AUTHORIT AUG 0 3 2001 HUNTER, Frederick D. ELI LILLY AND COMPANY ELI LILLY & COMPAR INTERNATION OF TRANSMITTAL OF PATENT DIVISION EXAMINATION REPORT Lilly Corporate Center Indianapolis, Indiana 46285 **ETATS-UNIS D'AMERIQUE** (PCT Rule 71.1) 317)276-3861 Date of mailing 27.07.2001 (day/month/year) Applicant's or agent's file reference IMPORTANT NOTIFICATION X-11600 Priority date (day/month/year) International filing date (day/month/year) International application No. 11/05/1999 PCT/US00/06707 09/05/2000 Applicant ELI LILLY AND COMPANY et al.

- 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

Authorized officer

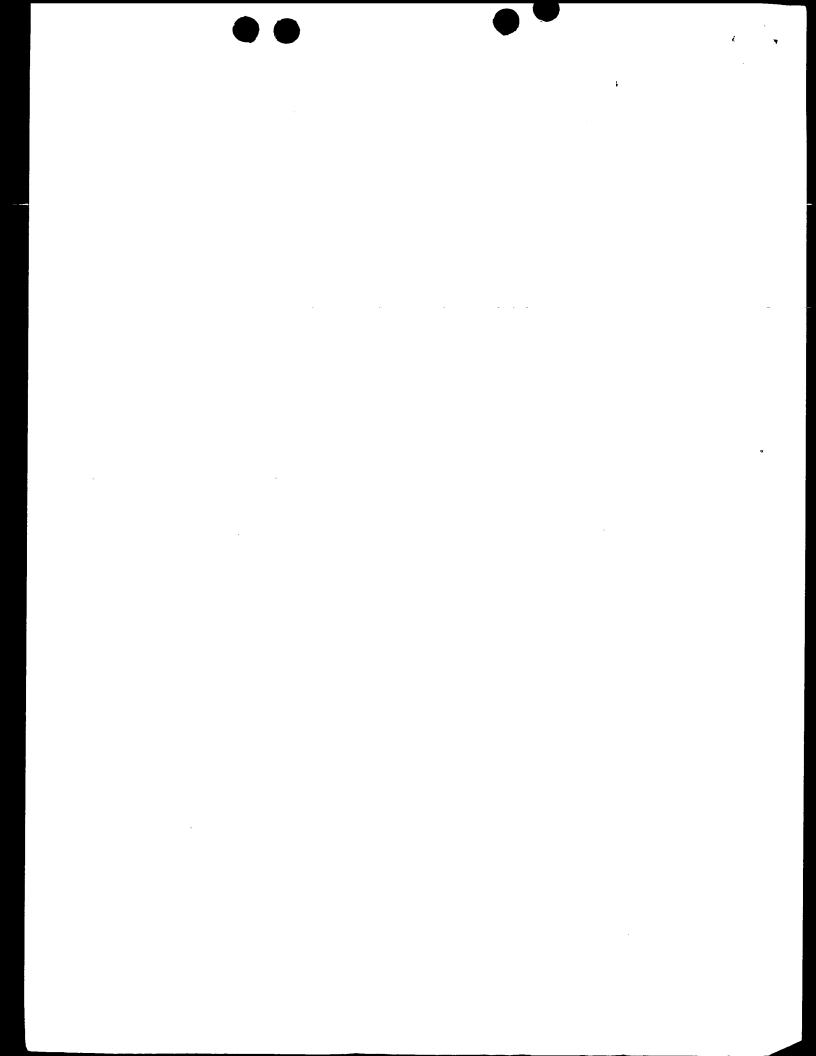
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx 523656 epmu d

Büchler, S

Fax: +49 89 2399 - 4465

Tel.+49 89 2399-8090





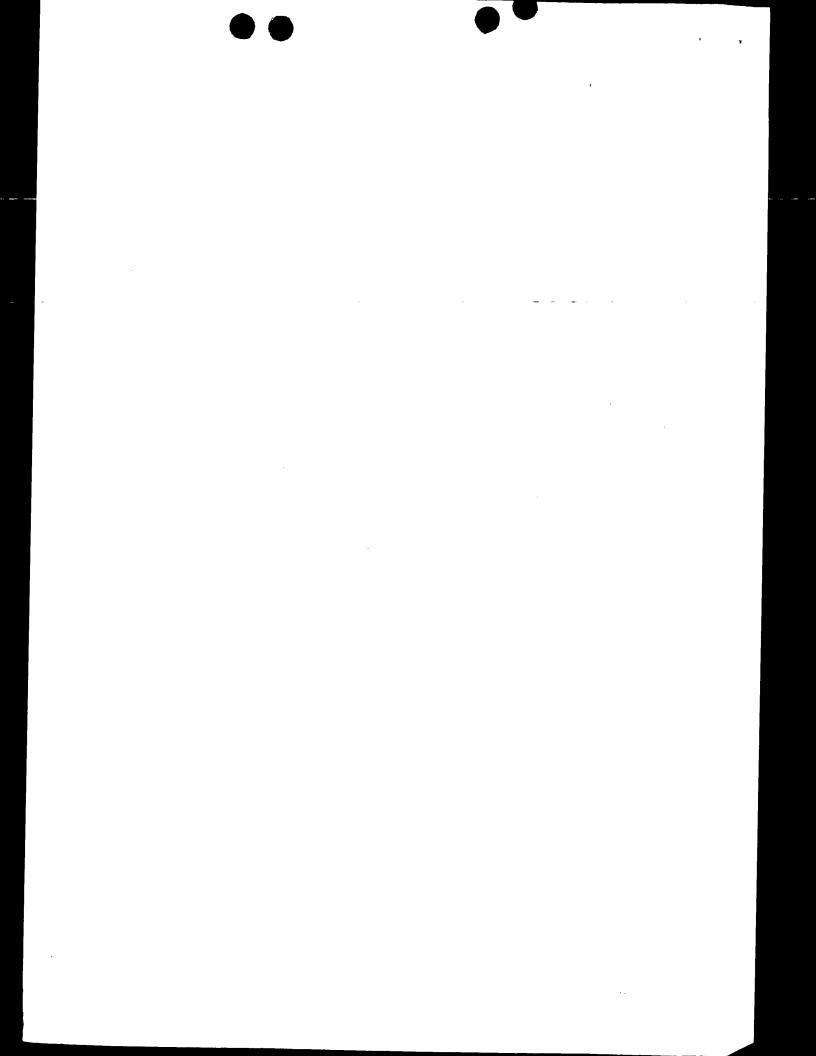
PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	COR CURTHER ACTION	See Notification of Transmittal of International FOR FURTHER ACTION Preliminary Examination Report (Form PCT/IPEA/416)					
X-11600							
International application No.	International filing date (day/month/year) Priority date (day/month/year) 11/05/1999						
PCT/US00/06707	09/05/2000	11/03/1999					
International Patent Classification (IPC) or na C07K14/47	tional classification and IPC						
Applicant							
ELI LILLY AND COMPANY et al.							
This international preliminary exam and is transmitted to the applicant a	nination report has been prepared according to Article 36.	d by this International Preliminary Examining Authority					
2. This REPORT consists of a total of	f 6 sheets, including this cover s	sheet.					
has amonded and are the ha	sis for this report and/or sheets to 207 of the Administrative Instruction	ne description, claims and/or drawings which have containing rectifications made before this Authority ions under the PCT).					
III 🖾 Non-establishment of	opinion with regard to novelty, ir	nventive step and industrial applicability					
IV ☐ Lack of unity of invent	tion						
v ⊠ Reasoned statement	- to a distance of the property inventive step or industrial applicability;						
VI Certain documents c							
VII Certain defects in the							
VIII Certain observations	on the international application						
Date of submission of the demand	Date o	of completion of this report					
13/11/2000	27.07	.2001					
Name and mailing address of the internation preliminary examining authority:	onal Autho	orized officer					
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 5230	656 epmu d	oradou, G					
Fax: +49 89 2399 - 4465		phone No. +49 89 2399 8543					

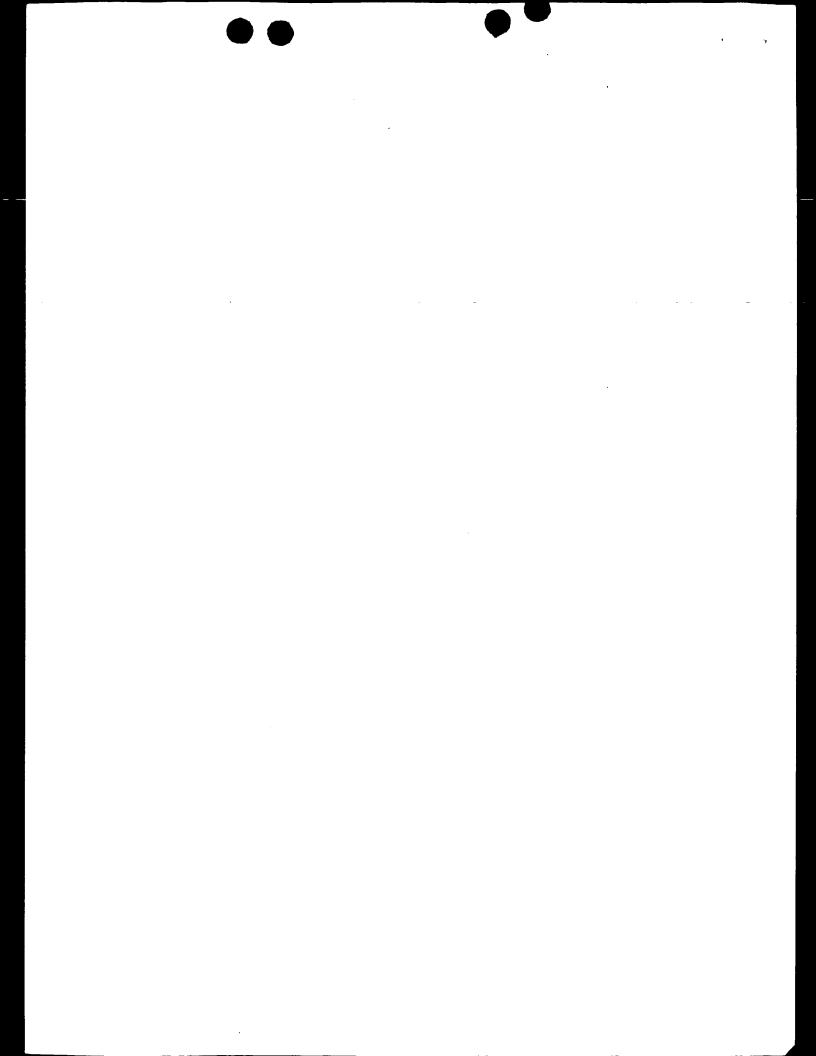


International application No. PCT/US00/06707

ı.	Bas	is of the report	
1.	the and	receiving Office in I	nents of the international application (Replacement sheets which have been furnished to response to an invitation under Article 14 are referred to in this report as "originally filed" this report since they do not contain amendments (Rules 70.16 and 70.17)):
	1-72	2	as originally filed
	Clai	ims, No.:	
	1-22	2	as originally filed
	Seq	uence listing part	of the description, pages:
	1-11	, filed with the lette	er of 07.08.2000
2.	With lang	n regard to the lang Juage in which the i	juage, all the elements marked above were available or furnished to this Authority in the international application was filed, unless otherwise indicated under this item.
	The	se elements were a	available or furnished to this Authority in the following language: , which is:
		the language of a	translation furnished for the purposes of the international search (under Rule 23.1(b)).
		the language of pu	ublication of the international application (under Rule 48.3(b)).
		the language of a 55.2 and/or 55.3).	translation furnished for the purposes of international preliminary examination (under Rule
3.			eleotide and/or amino acid sequence disclosed in the international application, the y examination was carried out on the basis of the sequence listing:
		contained in the in	ternational application in written form.
		filed together with	the international application in computer readable form.
	\boxtimes	furnished subsequ	ently to this Authority in written form.
	\boxtimes	furnished subsequ	ently to this Authority in computer readable form.
	×		it the subsequently furnished written sequence listing does not go beyond the disclosure in pplication as filed has been furnished.
	×	The statement that listing has been fu	It the information recorded in computer readable form is identical to the written sequence irnished.
4.	The	amendments have	e resulted in the cancellation of:
		the description,	pages:
		the claims,	Nos.:

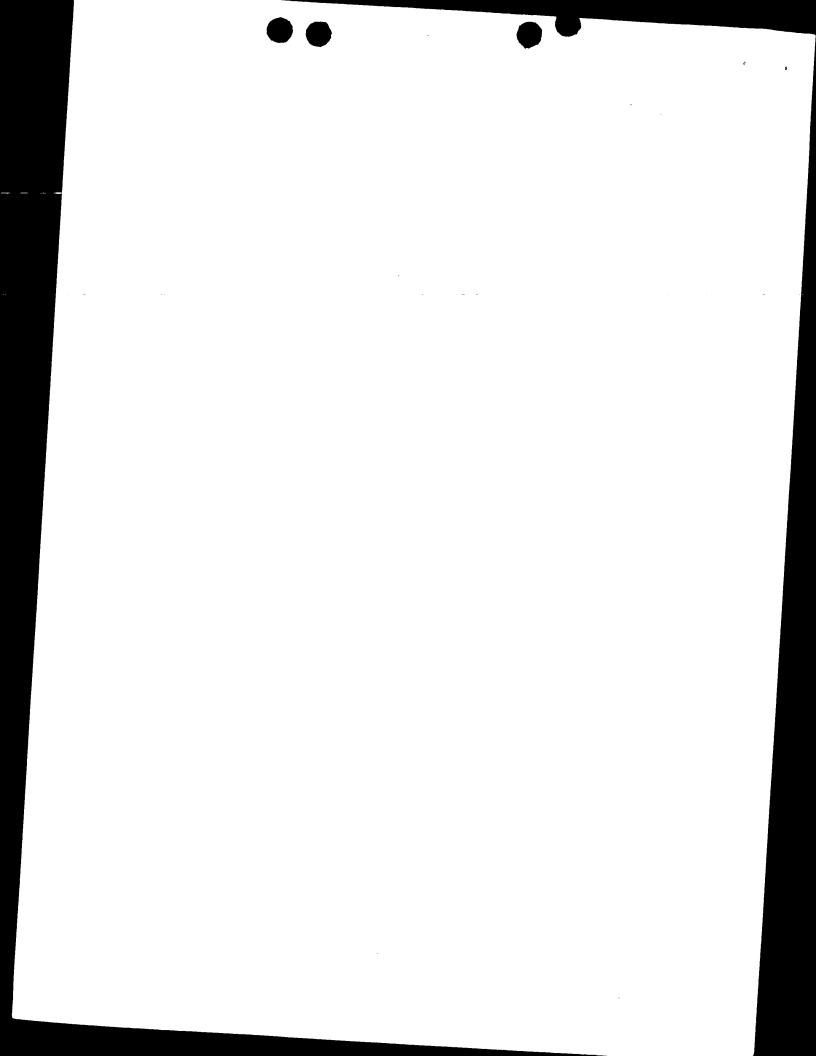
sheets:

☐ the drawings,



International application No. PCT/US00/06707

EXAMINATION	
5. This report has been established considered to go beyond the dis (Any replacement sheet contain report.)	l as if (some of) the amendments had not been made, since they have been closure as filed (Rule 70.2(c)): sing such amendments must be referred to under item 1 and annexed to this
6. Additional observations, if necessar	y:
 III. Non-establishment of opinion with the questions whether the claimed obvious), or to be industrially applied the entire international application. ☑ claims Nos. 21, 22. 	th regard to novelty, inventive step and industrial applicability invention appears to be novel, to involve an inventive step (to be non- cable have not been examined in respect of: tion.
because: the said international application and require an international p	tion, or the said claims Nos. relate to the following subject matter which does reliminary examination (specify):
that no meaning turopinion	awings (indicate particular elements below) or said claims Nos. are so unclear could be formed (specify):
could be formed. In original international prelications.	os. are so inadequately supported by the description that no meaningful opinion ort has been established for the said claims Nos. 21, 22. minary examination cannot be carried out due to the failure of the nucleotide ting to comply with the standard provided for in Annex C of the Administrative
the computer readable for	een furnished or does not comply with the standard. m has not been furnished or does not comply with the standard. Las revelty, inventive step or industrial applicability;
V. Reasoned statement under citations and explanations	Article 35(2) with regard to novelty, inventive step or industrial applicability; supporting such statement
Statement Novelty (N)	Yes: Claims 2, 3, 5-16, 18-20 No: Claims 1, 4, 17 Yes: Claims 2, 3, 5-16, 18-20
Inventive step (IS)	150.



International application No. PCT/US00/06707

No:

Claims 1, 4, 17

Industrial applicability (IA)

Yes:

Claims 1-20

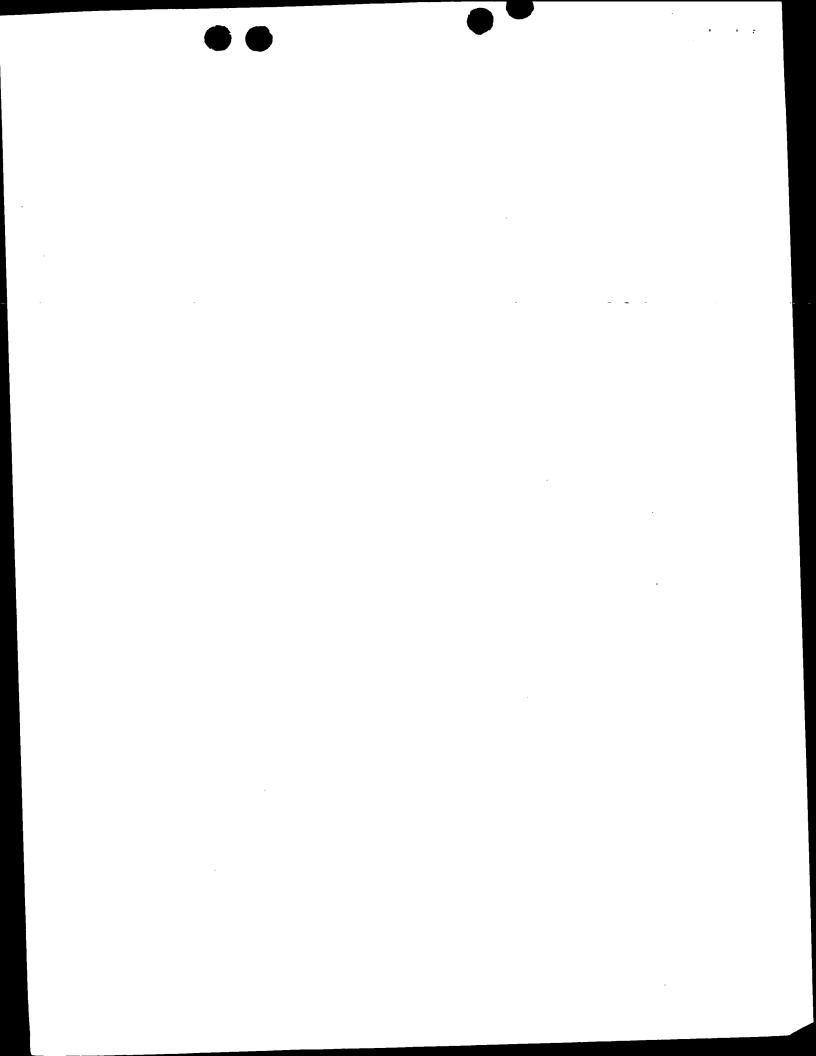
No:

: Claims

2. Citations and explanations see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made: see separate sheet



Reference is made to the following documents:

D1: WO 96 40885 A (MCCONLOGUE LISA C ;KEIM PAMELA S (US); SINHA SUKANTO (US); TAN HUA) 19 December 1996 (1996-12-19)

D2: DATABASE GENEMBL [Online] 6 June 1996 (1996-06-06) HILLIER ET AL.: 'yx480g8.r1 soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:265022 5' similar to contains Alu repetitive element' XP002148339

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1. D1 discloses the purification of a β-secretase protein. The starting material of D1 is identical to the starting material the present application, the β-secretase activity assay are similar and several purification steps are shared with the purification of the present application (see D1 pages 28 to 30 paragraph entitled "Purification and characterisation of β-secretase"). The partial sequences obtained from the protein of D1 seem not to be present in SEQ ID NO:2 or SEQ ID NO:4 of the present application therefore the proteins having said SEQ IDs appear to be novel with regard to the protein of D1. However the present claim 1 is drafted so broadly that its scope encompasses any protein being a "functional equivalent" of the proteins having said SEQ IDs without any limitation in sequence requirement (see also paragraph 5.). Therefore D1 is prejudicial for the novelty of claim 1.
- 2. The attention of the applicant is drawn to the fact that the SEQ ID NO:2 comprises a stretch of 27 undetermined amino acids. This implies that the statement "a fragment of at least 6 continuous amino acids thereof" in claim 1 encompasses all the fragments of the prior art having between 6 and 27 amino acids (Article 33.2 PCT).

In addition, the fragments "of at least 6 continuous amino acids" of claim 1 do not

appear to solve any technical problem. Consequently said fragments are merely considered as an arbitrary selection among all possible fragments of at least 6 amino acids. Therefore even in absence of undetermined amino acids in the SEQ ID NO: 2, claim 1 would be considered as lacking an inventive step (Article 33.3 PCT).

- 3. D2 discloses a sequence which is 97% identical to the sequence of SEQ ID NO:3 in 485 nucleotide overlap. A fragment having said sequence of D2 inherently selectively hybridises with the sequence of SEQ ID NO:3. D2 is therefore prejudicial for the novelty of claim 4 f).
- 4. D1 (page 41 line 16 to page 44 line 17) describes a β -secretase inhibitor assay utilizing purified β -secretase which anticipates claim 17 of the present application (Article 33.2 PCT).

Re Item VIII

Certain observations on the international application

- 5. The terms "functional equivalent" used in claim 1 are vague and unclear and leave the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
- 6. Claim 19 does not meet the criteria of Article 6 PCT. The present application does not provide a β-secretase different from the protein having the sequences shown in SEQ IDs No: 2 and 4. Therefore claim 19 is not supported by the description over its entire scope.
- 7. The same enzyme should not be given different names in the claims (Article 6 PCT). In claims 1, 4 and 11 the enzyme of the present application is named "an amyloid precursor protein protease" and in claims 17 to 20 said enzyme is referred to as a "β-secretase".

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IN THE UNITED STATES RECEIVING OFFICE (USRO)

Applicant(s): Gerald Wayne Becker

International Application No.: PCT/US00/06707

Filed: 05/09/2000 (05.09.00)

Invention: AMYLOID PRECURSOR PROTEIN PROTEASE AND RELATED NUCLEIC ACID

COMPOUNDS

Lilly Reference: X-11600

Earliest Priority Date: 05/11/1999 (05.11.1999)

Certificate Under 37 C.F.R. § 1.10

Attention: DO/EO

Box PCT

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir/Madam:

"Express Mail" mailing label number: __EL559725839US

Date of Deposit: <u>October 30, 2001</u>

I hereby certify that the following attached paper or fee

Transmittal Letter to the United States Designated/Elected Office (US) concerning a filing under 35 U.S.C. 371 of the International Application identified above is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

(Typed or printed name of person mailing paper)

Signature of person mailing paper or fee)

		•						
		•						



PCT

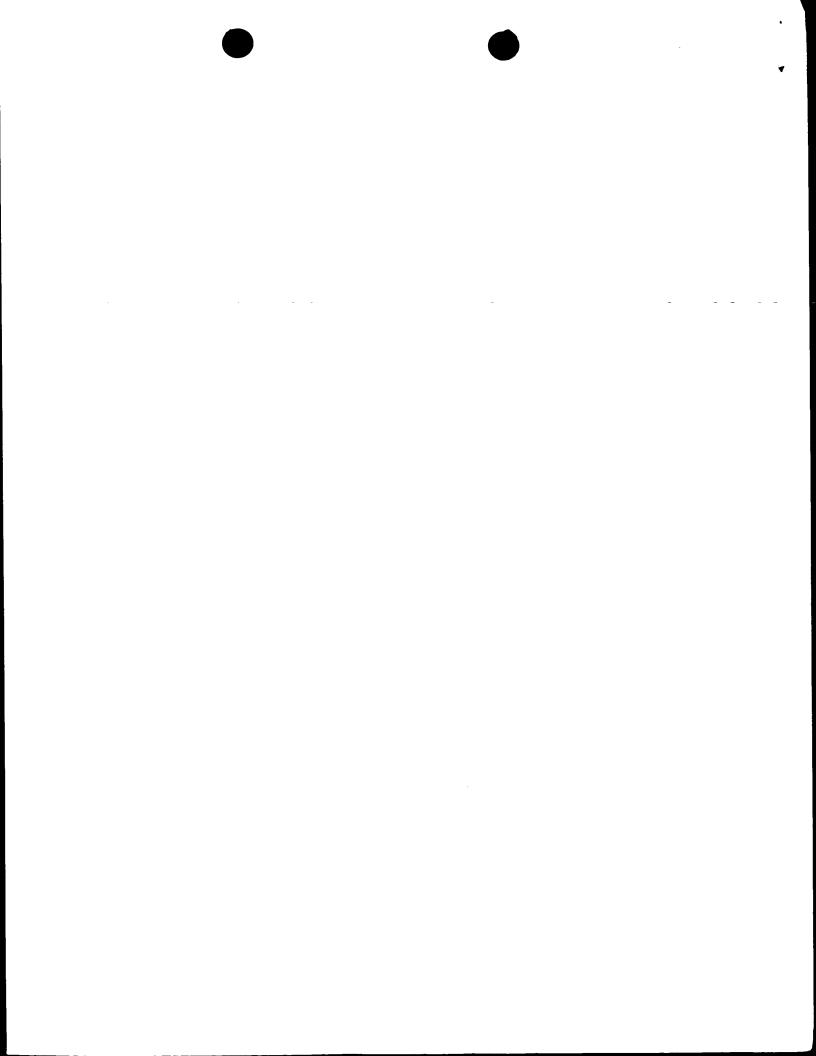
REC'D 3 1 JUL 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

				719
Applicant's	_	ent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
Internation		lication No	International filing date (day/moni	nth/year) Priority date (day/month/year)
PCT/US			09/05/2000	11/05/1999
			national classification and IPC	1
C07K14		shi olassilication (ii o) or	Transfer sidesmodifier and it s	
Applicant				
• •	V AN	D COMPANY et al.		
	- AN	D COMPANT et al.		
				ed by this International Preliminary Examining Authority
and i	s tran	smitted to the applicar	nt according to Article 36.	
2. This	REPO	ORT consists of a total	of 6 sheets, including this cover s	sheet.
	thin re	anastia alaa aaaamnas	aind by ANNEVES in shorts of t	the description, claims and/or drawings which have
				containing rectifications made before this Authority
(see F	Rule 70.16 and Section	607 of the Administrative Instruct	tions under the PCT).
Thes	e ann	exes consist of a total	of sheets	
11163	e aiiii	exes consist of a total	o, should.	
3. This	report	contains indications r	elating to the following items:	
	5-71			
	⊠ ⊠	Basis of the report		
		• •		and the second indication and indica
III IV		Lack of unity of inver	· ·	nventive step and industrial applicability
V	⊠	•		o novelty, inventive step or industrial applicability;
•	_		ations suporting such statement	o noverty, inventive step of industrial applicability,
VI		Certain documents	cited	
VII		Certain defects in the	e international application	
VIII	\boxtimes	Certain observations	on the international application	
Date of sul	missi	on of the demand	Date o	of completion of this report
13/11/20	00		27.07.2	2001
		g address of the internation in the state of the contraction in the state of the st	onal Authori	rized officer
		opean Patent Office		
<i>))</i>))		0298 Munich +49 89 2399 - 0 Tx: 523	Loubi	radou, G
		: +49 89 2399 - 4465	· · · · · · · · · · · · · · · · · · ·	none No. +49 89 2399 8543

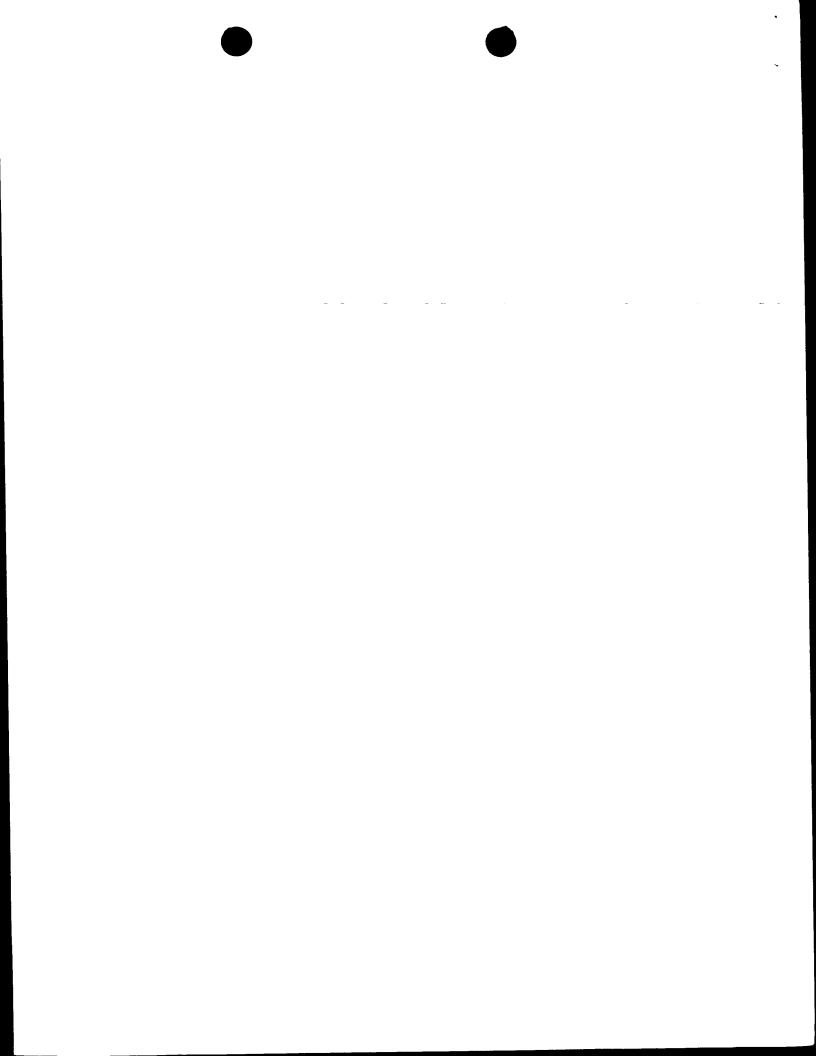




International application No. PCT/US00/06707

l. Bas	sis	of	the	re	por	t
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1.	With regard to the elements of the international application (Replacement sheets which have been furnished the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)): Description, pages:										
	1-7	2	as originally filed .								
	Claims, No.:										
	1-2	2	as originally filed								
	Sec	Sequence listing part of the description, pages:									
	1-1	I-11, filed with the letter of 07.08.2000									
2.	Witl lang	h regard to the lang guage in which the i	uage, all the elements marked above were available or furnished to this Authority in the nternational application was filed, unless otherwise indicated under this item.								
	The	These elements were available or furnished to this Authority in the following language: , which is:									
		the language of a t	ranslation furnished for the purposes of the international search (under Rule 23.1(b)).								
		the language of pu	blication of the international application (under Rule 48.3(b)).								
		the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).									
3.	With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:										
		contained in the int	rernational application in written form.								
		filed together with t	he international application in computer readable form.								
	\boxtimes	☑ furnished subsequently to this Authority in written form.									
	\boxtimes	☑ furnished subsequently to this Authority in computer readable form.									
	X	☑ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.									
	×	The statement that listing has been fur	the information recorded in computer readable form is identical to the written sequence nished.								
	The	amendments have	resulted in the cancellation of:								
		the description,	pages:								
		the claims,	Nos.:								
		the drawings,	sheets:								





International application No. PCT/US00/06707

					·					
5.		This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):								
		(Any replacement sheet report.)	contain	ing such	amendments must be referred to under item 1 and annexed to this					
6.	Add	litional observations, if ne	ecessary	/ :						
III.	Nor	n-establishment of opin	ion with	n regard t	to novelty, inventive step and industrial applicability					
1.	The obv	e questions whether the c rious), or to be industrially	laimed i applica	nvention able have	appears to be novel, to involve an inventive step (to be non- e not been examined in respect of:					
		the entire international a	pplication	on.						
	☑ claims Nos. 21, 22.									
be	caus	se:								
the said international application, or the said claims Nos. relate to the following subject matter which do not require an international preliminary examination (specify):										
	the description, claims or drawings (<i>indicate particular elements below</i>) or said claims Nos. are so unclear that no meaningful opinion could be formed (<i>specify</i>):									
		the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinior could be formed.								
	\boxtimes	☑ no international search report has been established for the said claims Nos. 21, 22.								
2.	A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:									
		the written form has not	been fu	urnished o	or does not comply with the standard.					
	the computer readable form has not been furnished or does not comply with the standard.									
V.	 V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability citations and explanations supporting such statement 									
1.	Sta	atement								
	No	velty (N)	Yes: No:		2, 3, 5-16, 18-20 1, 4, 17					
	lov	ventive sten (IS)	Yes.	Claims	2 3 5-16 18-20					

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		 -	



International application No. PCT/US00/06707

No:

Claims 1, 4, 17

Industrial applicability (IA)

Yes: Claims 1-20

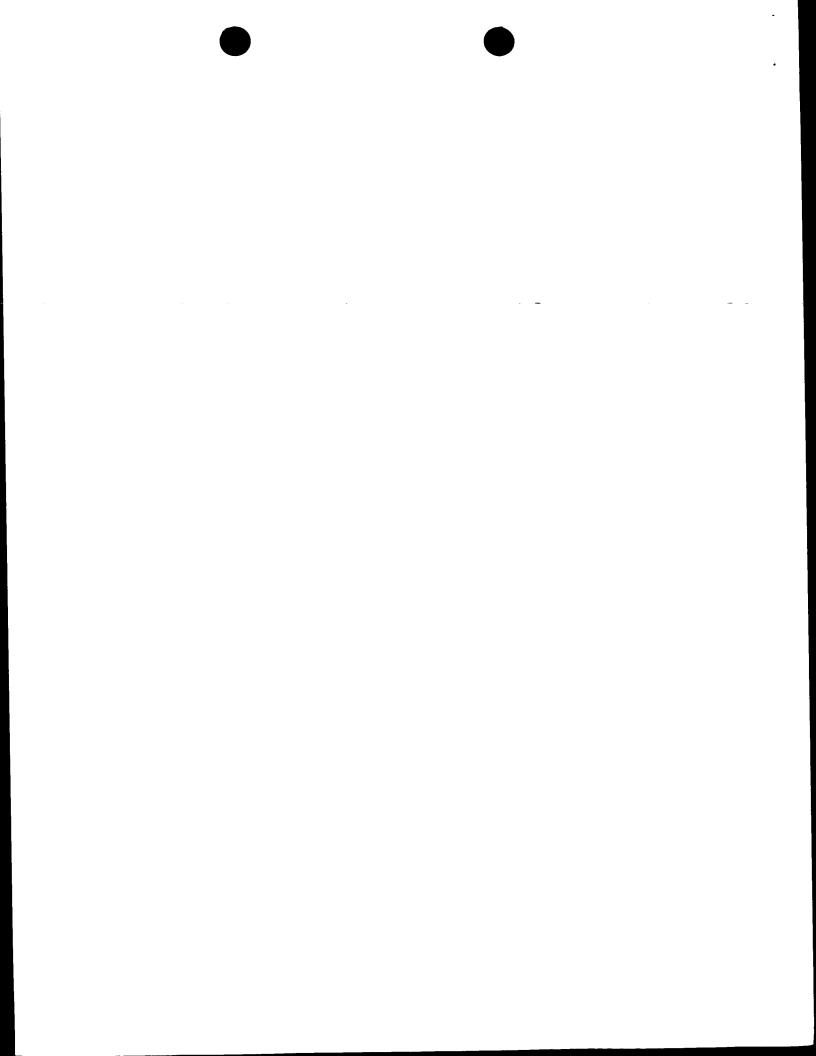
No:

Claims

2. Citations and explanations see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made: see separate sheet



Reference is made to the following documents:

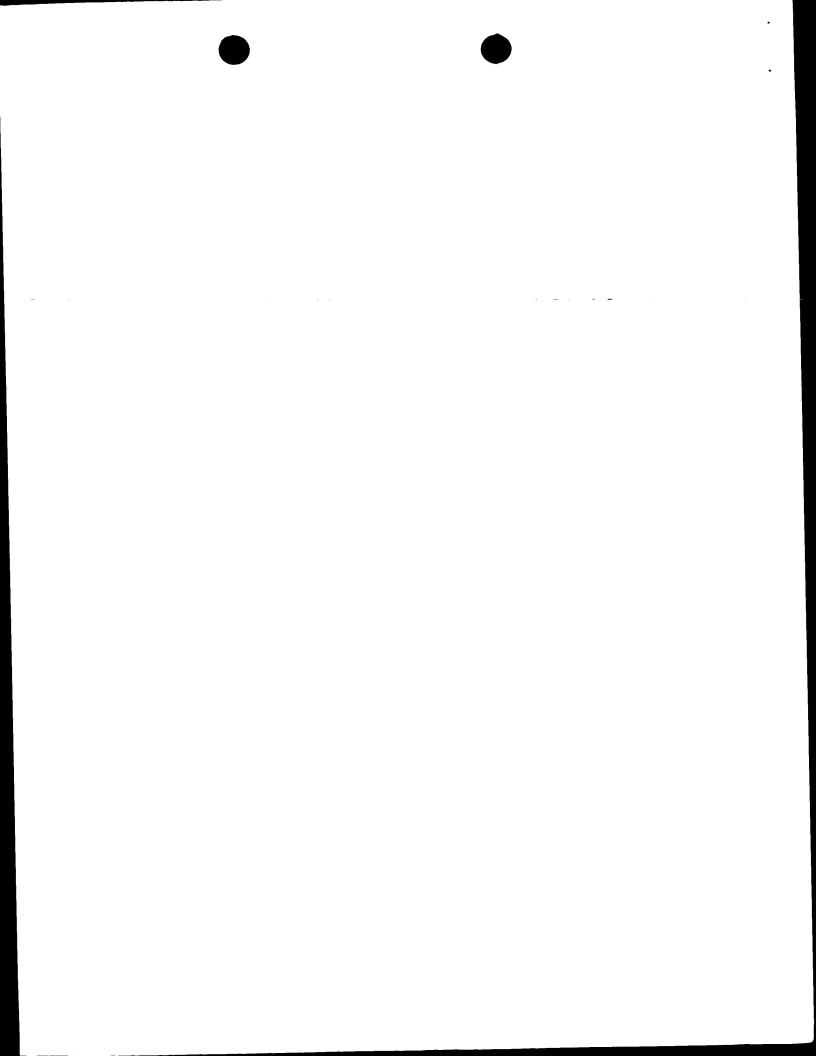
D1: WO 96 40885 A (MCCONLOGUE LISA C ;KEIM PAMELA S (US): SINHA SUKANTO (US); TAN HUA) 19 December 1996 (1996-12-19)

D2: DATABASE GENEMBL [Online] 6 June 1996 (1996-06-06) HILLIER ET AL.: 'yx480g8.r1 soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:265022 5' similar to contains Alu repetitive element' XP002148339

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1 discloses the purification of a β -secretase protein. The starting material of D1 1. is identical to the starting material the present application, the β -secretase activity assay are similar and several purification steps are shared with the purification of the present application (see D1 pages 28 to 30 paragraph entitled "Purification and characterisation of β -secretase"). The partial sequences obtained from the protein of D1 seem not to be present in SEQ ID NO:2 or SEQ ID NO:4 of the present application therefore the proteins having said SEQ IDs appear to be novel with regard to the protein of D1. However the present claim 1 is drafted so broadly that its scope encompasses any protein being a "functional equivalent" of the proteins having said SEQ IDs without any limitation in sequence requirement (see also paragraph 5.). Therefore D1 is prejudicial for the novelty of claim 1.
- 2. The attention of the applicant is drawn to the fact that the SEQ ID NO:2 comprises a stretch of 27 undetermined amino acids. This implies that the statement "a fragment of at least 6 continuous amino acids thereof" in claim 1 encompasses all the fragments of the prior art having between 6 and 27 amino acids (Article 33.2 PCT).
 - In addition, the fragments "of at least 6 continuous amino acids" of claim 1 do not





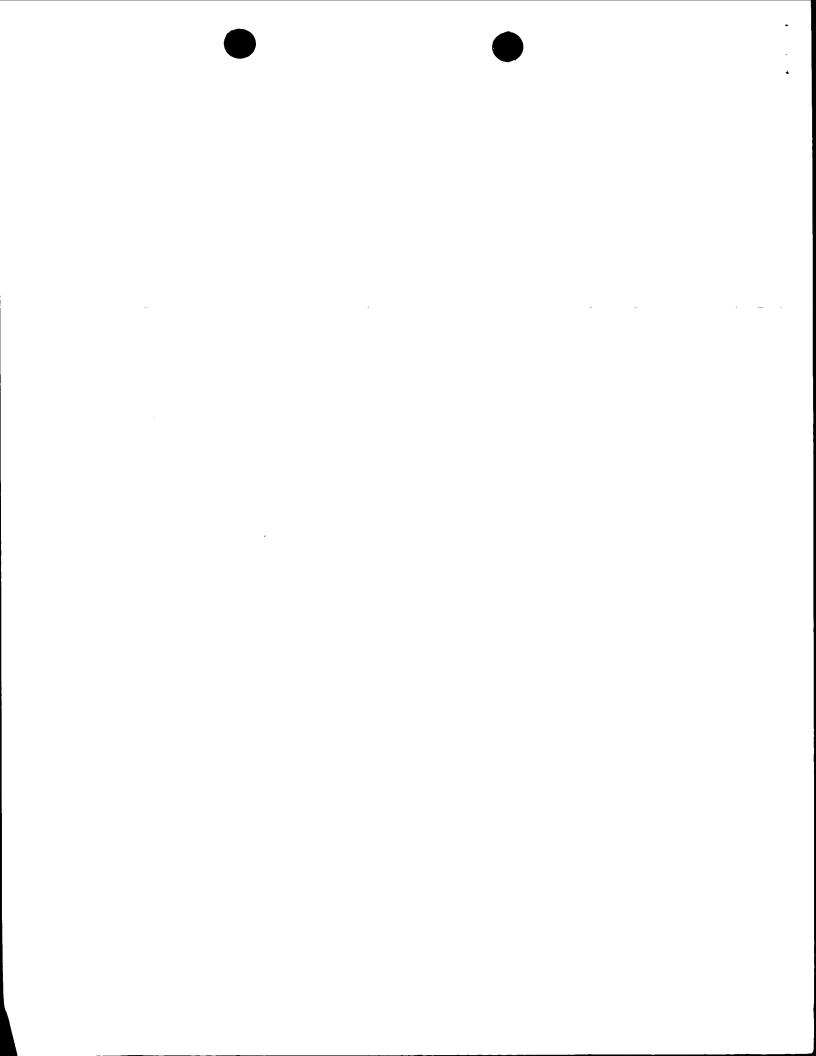
appear to solve any technical problem. Consequently said fragments are merely considered as an arbitrary selection among all possible fragments of at least 6 amino acids. Therefore even in absence of undetermined amino acids in the SEQ ID NO: 2, claim 1 would be considered as lacking an inventive step (Article 33.3 PCT).

- D2 discloses a sequence which is 97% identical to the sequence of SEQ ID NO:3 3. in 485 nucleotide overlap. A fragment having said sequence of D2 inherently selectively hybridises with the sequence of SEQ ID NO:3. D2 is therefore prejudicial for the novelty of claim 4 f).
- D1 (page 41 line 16 to page 44 line 17) describes a β -secretase inhibitor assay 4. utilizing purified β-secretase which anticipates claim 17 of the present application (Article 33.2 PCT).

Re Item VIII

Certain observations on the international application

- The terms "functional equivalent" used in claim 1 are vague and unclear and leave 5. the reader in doubt as to the meaning of the technical features to which they refer, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
- Claim 19 does not meet the criteria of Article 6 PCT. The present application does 6. not provide a β-secretase different from the protein having the sequences shown in SEQ IDs No: 2 and 4. Therefore claim 19 is not supported by the description over its entire scope.
- The same enzyme should not be given different names in the claims (Article 6 7. PCT). In claims 1, 4 and 11 the enzyme of the present application is named "an amyloid precursor protein protease" and in claims 17 to 20 said enzyme is referred to as a "β-secretase".



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A1

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5/16, A61P 25/28

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US

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(72) Inventors; and

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(74) Agents: WILSON, Alexander et al.; Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285 (US).

(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

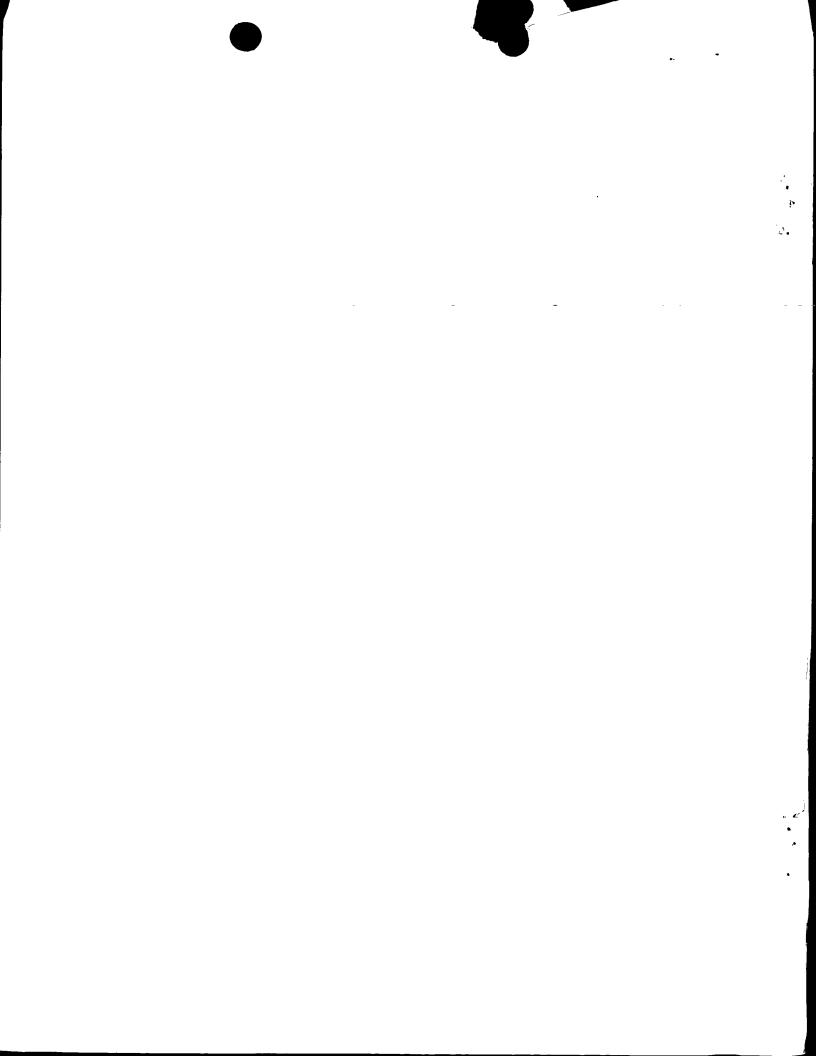
With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: AMYLOID PRECURSOR PROTEIN PROTEASE AND RELATED NUCLEIC ACID COMPOUNDS

(57) Abstract

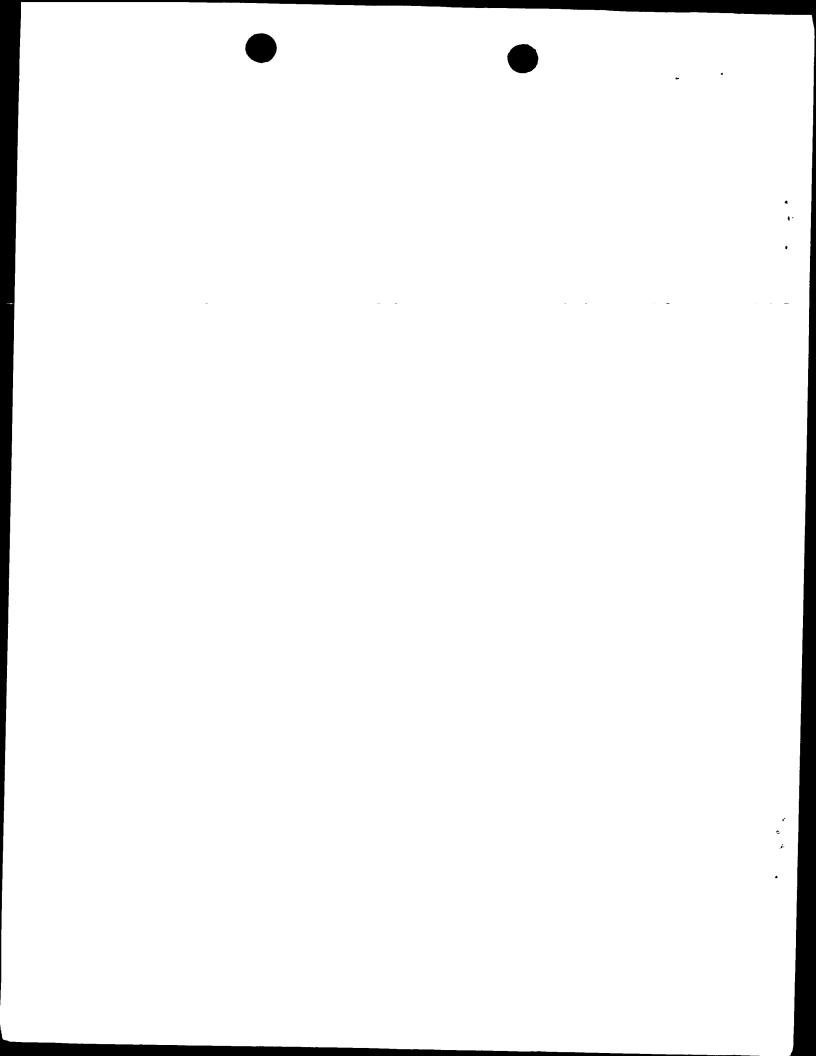
This present invention provides an amyloid precursor protein protease and related nucleic acid compounds thereof. The invention also provides compositions, expression vectors, and transfected host cells as well as assays and methods of use. The compounds of the present invention will further characterize Alzheimer's Disease and other neurodegenerative disease states.



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a. classification of subject matter IPC 7 C07K14/47 C12N15/57 A61P25/28

C12N9/64

C12N5/10

C12N5/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) $IPC \ 7 \quad C12N \quad C07K \quad A61P$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND, EMBL, GENSEQ, EPO-Internal

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE GENEMBL 'Online! 6 June 1996 (1996-06-06) HILLIER ET AL.: "yx480g8.rl soares melanocyte 2NbHM Homo sapiens cDNA clone IMAGE:265022 5' similar to contains Alu repetitive element" XP002148339 Accesion number N30496	1-16
X	WO 96 40885 A (MCCONLOGUE LISA C ;KEIM PAMELA S (US); SINHA SUKANTO (US); TAN HUA) 19 December 1996 (1996-12-19) page 22, line 20 -page 23, line 2 page 41, line 20 -page 48, line 34 claims 23-41; table 3	17

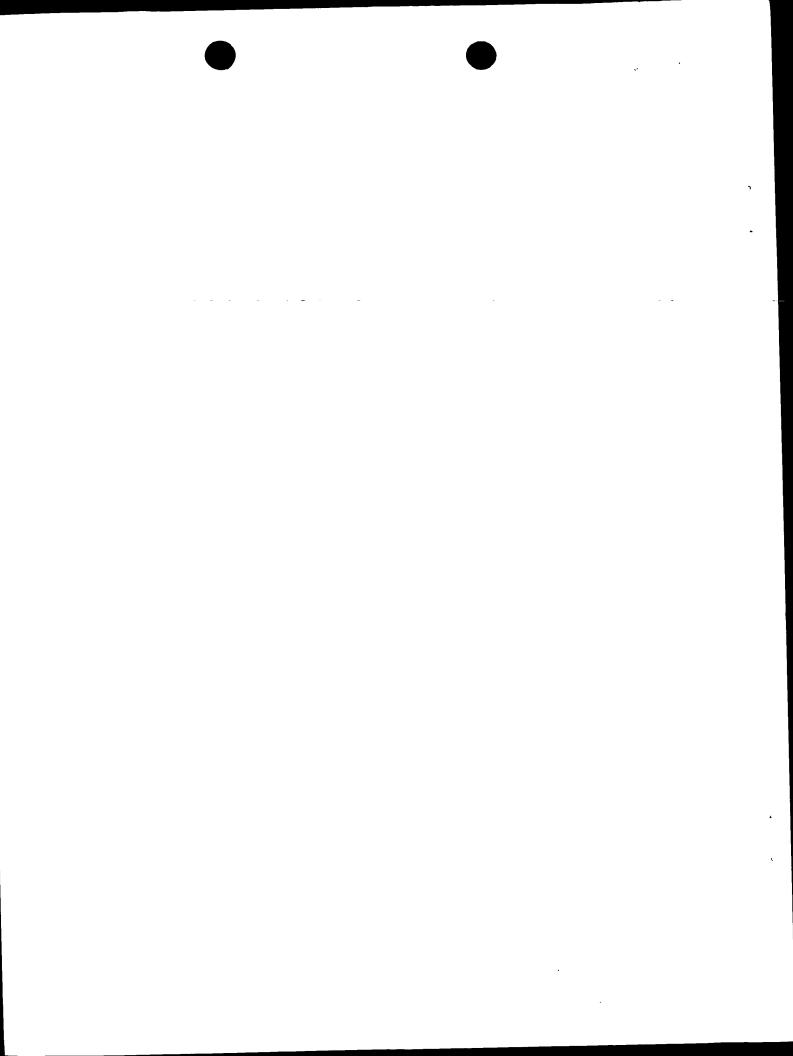
Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filling date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search 4 October 2000	Date of mailing of the international search report 17/10/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer ALCONADA RODRIG, A

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C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US 00/06707
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant
X	EP 0 653 154 A (HOECHST JAPAN) 17 May 1995 (1995-05-17) page 5, line 13-21 claim 10	Relevant to claim No.
4	DATABASE SWISSPROT 'Online! 1 June 1998 (1998-06-01) HUSAINI ET AL.: "Bos taurus butyrophilin fragment" XP002148340 Accession No. 046535	1-16
, X	WO 99 46281 A (BAKER KEVIN P; CHEN JIAN (US); GENENTECH INC (US); GURNEY AUSTIN () 16 September 1999 (1999-09-16) page 12, line 24-35 page 60, line 10-29 page 128, line 15-22 page 149, line 30-33 page 151, line 22-30 page 159, line 17-19	1-16



International Application No. PCT/US 00 \(D6707 \)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 21,22

Claims 21 and 22 refer to an antagonist/inhibitor of the polypeptide without giving a true technical characterization. Moreover, no such compunds are defined in the application. In consequence, the scope of said claims is ambigous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 6 PCT). No search could be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the result to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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ternation pplication No PCT/US 00/06707

	nt document search repor	t	Publication date		Patent family member(s)	Publication date
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				AU	1070399 A	10-05-1999
				EP	1025227 A	09-08-2000
				WO	9920756 A	29-04-1999

FIGURE 170A

GTCCCACATCCTGCTCAACTGGGTCAGGTCCCTCTTAGACCAGCTCTTGTCCATCATTTGCT GAAGTGGACCAACTAGTTCCCCAGTAGGGGGTCTCCCCTGGCAATTCTTGATCGGCGTTTGG TCTAACTATGGGACAAGGTTGTGCCGGCAGCTCTGGGGGAAGGAGCACGGGGCTGATCAAGC CATCCAGGAAACACTGGAGGACTTGTCCAGCCTTGAAAGAACTCTAGTGGTTTCTGAATCTA ${\tt GCCCACTTGGCGGTAAGC} \underline{{\tt ATG}} {\tt ATGCAACTTCTGCAACTTCTGCTGGGGCTTTTGGGGCCCAGG}$ TGGCTACTTATTTCTTTTAGGGGATTGTCAGGAGGTGACCACTCTCACGGTGAAATACCAAG TGTCAGAGGAAGTGCCATCTGGTACAGTGATCGGGAAGCTGTCCCAGGAACTGGGCCGGGAG GAGAGGCGGAGGCAAGCTGGGGCCCCCCCCCAT GCCGACAGTGGGATCCCTGCCTGGTTTCCTTTGATGTGCTTGCCACAGGGGATTTGGCTCTG ATCCATGTGGAGATCCAAGTGCTGGACATCAATGACCACCAGCCACGGTTTCCCAAAGGCGA GCAGGAGCTGGAAATCTCTGAGAGCGCCTCTCTGCGAACCCGGATCCCCCTGGACAGAGCTC TTGACCCAGACACAGGCCCTAACACCCTGCACACCTACACTCTGTCTCCCAGTGAGCACTTT GCCTTGGATGTCATTGTGGGCCCTGATGAGACCAAACATGCAGAACTCATAGTGGTGAAGGA GCTGGACAGGGAAATCCATTCATTTTTGATCTGGTGTTAACTGCCTATGACAATGGGAACC CCCCCAAGTCAGGTACCAGCTTGGTCAAGGTCAACGTCTTGGACTCCAATGACAATAGCCCT GCGTTTGCTGAGAGTTCACTGGCACTGGAAATCCAAGAAGATGCTGCACCTGGTACGCTTCT CATAAAACTGACCGCCACAGACCCTGACCAAGGCCCCAATGGGGAGGTGGAGTTCTTCCTCA GTAAGCACATGCCTCCAGAGGTGCTGGACACCTTCAGTATTGATGCCAAGACAGGCCAGGTC ATTCTGCGTCGACCTCTAGACTATGAAAAGAACCCTGCCTACGAGGTGGATGTTCAGGCAAG GGACCTGGGTCCCAATCCTATCCCAGCCCATTGCAAAGTTCTCATCAAGGTTCTGGATGTCA ATGACAACATCCCAAGCATCCACGTCACATGGGCCTCCCAGCCATCACTGGTGTCAGAAGCT CTTCCCAAGGACAGTTTTATTGCTCTTGTCATGGCAGATGACTTGGATTCAGGACACAATGG TTTGGTCCACTGCTGGCCGAGCCAAGAGCTGGGCCACTTCAGGCTGAAAAGAACTAATGGCA ACACATACATGTTGCTAACCAATGCCACACTGGACAGAGAGCAGTGGCCCAAATATACCCTC ACTCTGTTAGCCCAAGACCAAGGACTCCAGCCCTTATCAGCCAAGAAACAGCTCAGCATTCA GATCAGTGACATCAACGACAATGCACCTGTGTTTGAGAAAAGCAGGTATGAAGTCTCCACGC GGGAAAACAACTTACCCTCTCTTCACCTCATTACCATCAAGGCTCATGATGCAGACTTGGGC ATTAATGGAAAAGTCTCATACCGCATCCAGGACTCCCCAGTTGCTCACTTAGTAGCTATTGA CTCCAACACAGGAGGTCACTGCTCAGAGGTCACTGAACTATGAAGAGATGGCCGGCTTTG AGTTCCAGGTGATCGCAGAGGACAGCGGGCAACCCATGCTTGCATCCAGTGTCTCTGTG**T**GG GTCAGCCTCTTGGATGCCAATGATAATGCCCCAGAGGTGGTCCAGCCTGTGCTCAGCGATGG AAAAGCCAGCCTCTCCGTGCTTGTGAATGCCTCCACAGGCCACCTGCTGGTGCCCATCGAGA CTCCCAATGGCTTGGGCCCAGCGGGCACTGACACCTCCACTGGCCACTCACAGCTCCCGG CCATTCCTTTTGACAACCATTGTGGCAAGAGATGCAGACTCGGGGGCAAATGGAGAGCCCCT CTACAGCATCCGCAATGGAAATGAAGCCCACCTCTTCATCCTCAACCCTCATACGGGGCAGC GTAGAGGACCAGGGAAGCCCCCCTTACAGACCCGAGCCCTGTTGAGGGTCATGTTTGTCAC CAGTGTGGACCACCTGAGGGACTCAGCCCGCAAGCCTGGGGCCTTGAGCATGTCGATGCTGA CGGTGATCTGCCTGGCTGTACTGTTGGGCATCTTCGGGTTGATCCTGGCTTTGTTCATGTCC ATCTGCCGGACAGAAAAGAAGGACAACAGGGCCTACAACTGTCGGGAGGCCGAGTCCACCTA CCGCCAGCAGCCCAAGAGGCCCCAGAAACACATTCAGAAGGCAGACATCCACCTCGTGCCTG TGCTCAGGGGTCAGGCAGGTGAGCCTTGTGAAGTCGGGCAGTCCCACAAAGATGTGGACAAG GAGGCGATGATGGAAGCAGGCTGGGACCCCTGCCTGCAGGCCCCCTTCCACCTCACCCGAC CCTGTACAGGACGCTGCGTAATCAAGGCAACCAGGGAGCACCGGCGGAGAGCCGAGAGGTGC TGCAAGACACGGTCAACCTCCTTTTCAACCATCCCAGGCAGAGGAATGCCTCCCGGGAGAAC CTGAACCTTCCCGAGCCCAGCCTGCCACAGGCCAGCCACGTTCCAGGCCTCTGAAGGTTGC AGGCAGCCCCACAGGGAGGCTGGAGACCAGGGCAGTGAGGAAGCCCCACAGAGGCCAC CAGCCTCCTCTGCAACCCTGAGACGGCAGCGACATCTCAATGGCAAAGTGTCCCCTGAGAAA GCGGAACCCCGTGGAGGAGCTCACTGTGGATTCTCCTCTGTTCAGCAAATCTCCCAGCTGC TGTCCTTGCTGCATCAGGGCCAATTCCAGCCCAAACCAAACCACCGAGGAAATAAGTACTTG GCCAAGCCAGGAGGCAGGAGTGCAATCCCAGACAGATGGCCCAAGTGCAAGGGCTGG

FIGURE 170B

AGGCCAGACAGACCCAGAACAGGAGGAGGAGGCCTTTGGATCCTGAAGAGGACCTCTCTGTGA AGCAACTGCTAGAAGAAGAGCTGTCAAGTCTGCTGGACCCCAGCACAGGTCTGGCCCTGGAC CGGCTGAGCGCCCTGACCCGGCCTGGATGGCGAGACTCTCTTTGCCCCTCACCACCAACTA CCGTGACAATGTGATCTCCCCGGATGCTGCAGCCACGGAGGAGCCGAGGACCTTCCAGACGT TCGGCAAGGCAGAGCCAGAGCTGAGCCCAACAGGCACGAGGCTGGCCAGCACCTTTGTC TCGGAGATGAGCTCACTGCTGGAGATGCTGCTGGAACAGCGCTCCAGCATGCCCGTGGAGGC CGCCTCCGAGGCGCTGCGGCGCTCTCGGTCTGCGGGAGGACCCTCAGTTTAGACTTGGCCA CCAGTGCAGCCTCAGGCATGAAAGTGCAAGGGGACCCAGGTGGAAAGACGGGGACTGAGGGC AAGAGCAGAGCAGCAGCAGCAGCAGCTGCCTGTGAACATACCTCAGACGCCTCTGGAT CCAAGAACCAGGGGCCTGAGGATCTGTGGACAAGAGCTGGTTTCTAAAATCTTGTAACTCAC TAGCTAGCGGCGGCCTGAGAACTTTAGGGTGACTGATGCTACCCCCACAGAGGGGGCAAGAG CCCCAGGACTAACAGCTGACTGACCAAAGCAGCCCCTTGTAAGCAGCTCTGAGTCTTTTGGA GGACAGGGACGGTTTGTGGCTGAGATAAGTGTTTCCTGGCAAAACATATGTGGAGCACAAAG GGGTAGCAGGAGTCAGGGGGCTGTACCCTGGGGGTGCCAGGAAATGCTCTCTGACCTATCAA TAAAGGAAAAGCAGTAAAAAAAAAAAAAAAAAAAAA

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48331

<subunit 1 of 1, 1184 aa, 1 stop</pre>

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Important features:

Signal peptide:

amino acids 1-13

Transmembrane domain:

amino acids 719-739

N-glycosylation site.

amino acids 415-418, 582-585, 659-662, 662-665 amd 857-860

Cadherins extracellular repeated domain signature.

amino acids 123-133, 232-242, 340-350, 448-458 and 553-563

174/237

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FIGURE 172

CGGACGCGTGGGCGGACGCGTGGGGGAGAGCCGCAGTCCCGGCTGCAGCACCTGGGAGAAGG CAGACCGTGTGAGGGGGCCTGTGGCCCCAGCGTGCTGTGGCCTCGGGGAGTGGGAAGTGGAG GCAGGAGCCTTCCTTACACTTCGCCATGAGTTTCCTCATCGACTCCAGCATCATGATTACCT CCCAGATACTATTTTTGGATTTGGGTGGCTTTTCTTCATGCGCCAATTGTTTAAAGACTAT GAGATACGTCAGTATGTTGTACAGGTGATCTTCTCCGTGACGTTTGCATTTTCTTGCACCAT GTTTGAGCTCATCTTTTGAAATCTTAGGAGTATTGAATAGCAGCTCCCGTTATTTTCACT GGAAAATGAACCTGTGTGTAATTCTGCTGATCCTGGTTTTCATGGTGCCTTTTTACATTGGC TATTTTATTGTGAGCAATATCCGACTACTGCATAAACAACGACTGCTTTTTTCCTGTCTCTT ATGGCTGACCTTTATGTATTTCTTCTGGAAACTAGGAGATCCCTTTCCCATTCTCAGCCCAA **AACATGGGATCTTATCCATAGAACAGCTCATCAGCCGGGTTGGTGATTGGAGTGACTCTC** ATGGCTCTTCTTCTGGATTTGGTGCTGTCAACTGCCCATACACTTACATGTCTTACTTCCT CAGGAATGTGACTGACACGGATATTCTAGCCCTGGAACGGCGACTGCTGCAAACCATGGATA TGATCATAAGCAAAAAGAAAAGGATGGCAATGGCACGGAGAACAATGTTCCAGAAGGGGGAA GTGCATAACAAACCATCAGGTTTCTGGGGAATGATAAAAAGTGTTACCACTTCAGCATCAGG TTTTTCTGGAAACAGCTGATCTATATGCTACCAAGGAGAGAATAGAATACTCCAAAACCTTC **AAGGGGAAATATTTTAATTTTCTTGGTTACTTTTTCTCTATTTACTGTGTTTTGGAAAATTTT** CATGGCTACCATCAATATTGTTTTTGATCGAGTTGGGAAAACGGATCCTGTCACAAGAGGCA TTGAGATCACTGTGAATTATCTGGGAATCCAATTTGATGTGAAGTTTTGGTCCCAACACATT TCCTTCATTCTTGTTGGAATAATCATCGTCACATCCATCAGAGGATTGCTGATCACTCTTAC CAAGTTCTTTTATGCCATCTCTAGCAGTAAGTCCTCCAATGTCATTGTCCTGCTATTAGCAC AGATAATGGGCATGTACTTTGTCTCCTCTGTGCTGATCCGAATGAGTATGCCTTTAGAA TACCGCACCATAATCACTGAAGTCCTTGGAGAACTGCAGTTCAACTTCTATCACCGTTGGTT TGATGTGATCTTCCTGGTCAGCGCTCTCTCTAGCATACTCTTCCTCTATTTGGCTCACAAAC AGGCACCAGAGAAGCAAATGGCACCTTGAACTTAAGCCTACTACAGACTGTTAGAGGCCAGT GGTTTCAAAATTTAGATATAAGAGGGGGGAAAAATGGAACCAGGGCCTGACATTTTATAAAC **AAACAAAATGCTATGGTAGCATTTTTCACCTTCATAGCATACTCCTTCCCCGTCAGGTGATA** GCAGAGAGCATCCCGTGTGGATATGAGGCTGGTGTAGAGGCGGAGAGGAGCCAAGAAACTAA AGGTGAAAAATACACTGGAACTCTGGGGCAAGACATGTCTATGGTAGCTGAGCCAAACACGT AGGATTTCCGTTTTAAGGTTCACATGGAAAAGGTTATAGCTTTGCCTTGAGATTGACTCATT **ACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAATG**

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MSFLIDSSIMITSQILFFGFGWLFFMRQLFKDYEIRQYVVQVIFSVTFAFSCTMFELIIFEI
LGVLNSSSRYFHWKMNLCVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTFMYFF
WKLGDPFPILSPKHGILSIEQLISRVGVIGVTLMALLSGFGAVNCPYTYMSYFLRNVTDTDI
LALERRLLQTMDMIISKKKRMAMARRTMFQKGEVHNKPSGFWGMIKSVTTSASGSENLTLIQ
QEVDALEELSRQLFLETADLYATKERIEYSKTFKGKYFNFLGYFFSIYCVWKIFMATINIVF
DRVGKTDPVTRGIEITVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLITLTKFFYAISS
SKSSNVIVLLLAQIMGMYFVSSVLLIRMSMPLEYRTIITEVLGELQFNFYHRWFDVIFLVSA
LSSILFLYLAHKQAPEKQMAP

Important features:

Signal peptide:

amino acids 1-23

Potential transmembrane domains:

amino acids 37-55, 81-102, 150-168, 288-311, 338-356, 375-398, 425-444

N-glycosylation sites.

amino acids 67-70, 180-183 and 243-246

Eukaryotic cobalamin-binding proteins

amino acids 151-160

CATGGGAAGTGGAGCCGGAGCCTTCCTTACACTCGCCATGAGTTTCCTCATCGACTCCAGCA
TCATGATTACCTCCCNGANACTATTTTTTGGATTTGGGTGGCTTTTCTTCNGCGCCAATGTT
TAAAGACTATGAGATACGTCAGTATGTTGTACNGGTGATCTTCTCCGTGACGTTTGCCATTT
CTTGCACCATGTTTGAGCTCATCATCTTTGAAATCTTNGGAGTATTGAATAGCAGCTCCCGT
TATTTTCACTGGAAAATGAACCTGTGTGTAATTCTGCTGATCCTGGTTNTCATGGTGCCTTT
TTACATTGGCTATTTTATTGTGAGCAATATCCGACTACTGCATAAACAACGACTGCTTTTTT
CCTGTCTCTTATGGCTGACCTTTATGTATTTCCAG

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FIGURE 175

FIGURE 176A

 ${\tt CTCGCGCAGGGATCGTCCC} \underline{{\tt ATG}} {\tt GCCGGGGCTCGGAGCCGCGACCCTTGGGGGGCCTCCGGGA}$ TTTGCTACCTTTTTGGCTCCTGCTCGTCGAACTGCTCTTCTCACGGGCTGTCGCCTTCAAT CTGGACGTGATGGGTGCCTTGCGCAAGGAGGGCGAGCCAGGCAGCCTCTTCGGCTTCTCTGT CCCTGGCTCTTCCTGGGCAGCAGCGAATCGCACTGGAGGCCTCTTCGCTTGCCCGTTGAGC CTGGAGGAGACTGACTGCTACAGAGTGGACATCGACCAGGGAGCTGATATGCAAAAGGAAAG CAAGGAGAACCAGTGGTTGGGAGTCAGTGTTCGGAGCCAGGGGCCTGGGGGCAAGATTGTTA CCTGTGCACACCGATATGAGGCAAGGCAGCGAGTGGACCAGATCCTGGAGACGCGGGATATG ATTGGTCGCTGCTTTGTGCTCAGCCAGGACCTGGCCATCCGGGATGAGTTGGATGGTGGGGA ATGGAAGTTCTGTGAGGGACGCCCCCAAGGCCATGAACAATTTGGGTTCTGCCAGCAGGGCA CAGCTGCCGCCTTCTCCCCTGATAGCCACTACCTCCTCTTTGGGGCCCCAGGAACCTATAAT TGGAAGGGCACGGCCAGGGTGGAGCTCTGTGCACAGGGCTCAGCGGACCTGGCACACCTGGA CGACGGTCCCTACGAGGCGGGGGGAGAGAAGGAGCAGGACCCCCGCCTCATCCCGGTCCCTG AGCTTTGTGGCTGGAGCCCCCCCCCCCCAACCAAGGGTGCTGTGGTCATCCTGCGCAAGGA CAGCGCCAGTCGCCTGGTGCCCGAGGTTATGCTGTCTGGGGAGCGCCTGACCTCCGGCTTTG CCCTACTTCTTTGAGCGCCAAGAAGAGCTGGGGGGGTGCTGTGTATGTGTACTTGAACCAGGG GGGTCACTGGGGTTCTCCCCTCTCCGGCTCTGCGGCTCCCCTGACTCCATGTTCGGGA TCAGCCTGGCTGTCCTGGGGGACCTCAACCAAGATGGCTTTCCAGATATTGCAGTGGGTGCC CCCTTTGATGGTGATGGGAAAGTCTTCATCTACCATGGGAGCAGCCTGGGGGTTGTCGCCAA ACCTTCACAGGTGCTGGAGGGCGAGGCTGTGGGCATCAAGAGCTTCGGCTACTCCCTGTCAG GCAGCTTGGATATGGATGGGAACCAATACCCTGACCTGCTGGTGGGCTCCCTGGCTGACACC GCAGTGCTCTTCAGGGCCAGACCCATCCTCCATGTCTCCATGAGGTCTCTATTGCTCCACG AAGCATCGACCTGGAGCAGCCCAACTGTGCTGGCGGCCCACTCGGTCTGTGTGGACCTAAGGG TCTGTTTCAGCTACATTGCAGTCCCCAGCAGCTATAGCCCTACTGTGGCCCTGGACTATGTG TTAGATGCGGACACAGACCGGAGGCTCCGGGGCCAGGTTCCCCGTGTGACGTTCCTGAGCCG TAACCTGGAAGAACCCAAGCACCAGGCCTCGGGCACCGTGTGGCTGAAGCACCAGCATGACC GAGTCTGTGGAGACGCCATGTTCCAGCTCCAGGAAAATGTCAAAGACAAGCTTCGGGCCATT GTAGTGACCTTGTCCTACAGTCTCCAGACCCCTCGGCTCCGGCGACAGGCTCCTGGCCAGGG ACTTCCTGAAGCAAGGCTGTGGTGAAGACAAGATCTGCCAGAGCAATCTGCAGCTGGTCCAC GCCCGCTTCTGTACCCGGGTCAGCGACACGGAATTCCAACCTCTGCCCATGGATGTGGATGG AACAACAGCCCTGTTTGCACTGAGTGGGCAGCCAGTCATTGGCCTGGAGCTGATGGTCACCA ACCTGCCATCGGACCCAGCCCCAGGCTGATGGGGATGATGCCCATGAAGCCCAGCTC CTGGTCATGCTTCCTGACTCACTGCACTACTCAGGGGTCCGGGGCCCTGGACCCTGCGGAGAA GCCACTCTGCCTGTCCAATGAGAATGCCTCCCATGTTGAGTGTGAGCTGGGGGAACCCCATGA AGAGAGGTGCCCAGGTCACCTTCTACCTCATCCTTAGCACCTCCGGGATCAGCATTGAGACC ACGGAACTGGAGGTAGAGCTGCTGTTGGCCACGATCAGTGAGCAGGAGCTGCATCCAGTCTC TGCACGAGCCCGTGTCTTCATTGAGCTGCCACTGTCCATTGCAGGAATGGCCATTCCCCAGC AACTCTTCTTCTCTGGTGTGGGGGGGGGGGGAGAGAGCCATGCAGTCTGAGCGGGATGTGGGC AGCAAGGTCAAGTATGAGGTCACGGTTTCCAACCAAGGCCAGTCGCTCAGAACCCTGGGCTC TGCCTTCCTCAACATCATGTGGCCTCATGAGATTGCCAATGGGAAGTGGTTGCTGTACCCAA TGCAGGTTGAGCTGGAGGGCGGGCAGGGGCCTGGGCAGAAAGGGCTTTGCTCTCCCAGGCCC GCAGCAGGAGCCTGGTGAGCGGCAGGAGCCCAGCATGTCCTGGTGGCCAGTGTCCTCTGCTG TGCCCACTCTACAGCTTTGACCGCGCGCGCTGTGCTGCATGTCTGGGGCCGTCTCTGGAACAG CACCTTTCTGGAGGAGTACTCAGCTGTGAAGTCCCTGGAAGTGATTGTCCGGGCCAACATCA CAGTGAAGTCCTCCATAAAGAACTTGATGCTCCGAGATGCCTCCACAGTGATCCCAGTGATG GTATACTTGGACCCCATGGCTGGTGGCCAGAAGGAGTGCCCTGGTGGGTCATCCTCCTGGC TGTACTGGCTGGCTGCTGGTGCTAGCACTGCTGGTGCTCCTGTGGAAGATGGGATTCT TCAAACGGGCGAAGCACCCGAGGCCACCGTGCCCCAGTACCATGCGGTGAAGATTCCTCGG GAAGACCGACAGCAGTTCAAGGAGGAGAAGACGGGCACCATCCTGAGGAACAACTGGGGCAG

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FIGURE 176B

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA55737

><subunit 1 of 1, 1141 aa, 1 stop

><MW: 124671, pI: 5.82, NX(S/T): 5

MAGARSRDPWGASGICYLFGSLLVELLFSRAVAFNLDVMGALRKEGEPGSLFGFSVALHRQL QPRPQSWLLVGAPQALALPGQQANRTGGLFACPLSLEETDCYRVDIDQGADMQKESKENQWL GVSVRSQGPGGKIVTCAHRYEARQRVDQILETRDMIGRCFVLSQDLAIRDELDGGEWKFCEG RPQGHEQFGFCQQGTAAAFSPDSHYLLFGAPGTYNWKGTARVELCAQGSADLAHLDDGPYEA GGEKEQDPRLIPVPANSYFGFSIDSGKGLVRAEELSFVAGAPRANHKGAVVILRKDSASRLV PEVMLSGERLTSGFGYSLAVADLNSDGWPDLIVGAPYFFERQEELGGAVYVYLNQGGHWAGI SPLRLCGSPDSMFGISLAVLGDLNQDGFPDIAVGAPFDGDGKVFIYHGSSLGVVAKPSQVLE GEAVGIKSFGYSLSGSLDMDGNQYPDLLVGSLADTAVLFRARPILHVSHEVSIAPRSIDLEQ PNCAGGHSVCVDLRVCFSYIAVPSSYSPTVALDYVLDADTDRRLRGQVPRVTFLSRNLEEPK ${\tt HQASGTVWLKHQHDRVCGDAMFQLQENVKDKLRAIVVTLSYSLQTPRLRRQAPGQGLPPVAP}$ ILNAHQPSTQRAEIHFLKQGCGEDKICQSNLQLVHARFCTRVSDTEFQPLPMDVDGTTALFA LSGQPVIGLELMVTNLPSDPAQPQADGDDAHEAQLLVMLPDSLHYSGVRALDPAEKPLCLSN ENASHVECELGNPMKRGAQVTFYLILSTSGISIETTELEVELLLATISEQELHPVSARARVF IELPLSIAGMAIPQQLFFSGVVRGERAMQSERDVGSKVKYEVTVSNQGQSLRTLGSAFLNIM WPHEIANGKWLLYPMQVELEGGQGPGQKGLCSPRPNILHLDVDSRDRRRRELEPPEQQEPGE RQEPSMSWWPVSSAEKKKNITLDCARGTANCVVFSCPLYSFDRAAVLHVWGRLWNSTFLEEY SAVKSLEVIVRANITVKSSIKNLMLRDASTVIPVMVYLDPMAVVAEGVPWWVILLAVLAGLL VLALLVLLLWKMGFFKRAKHPEATVPQYHAVKIPREDRQQFKEEKTGTILRNNWGSPRREGP DAHPILAADGHPELGPDGHPGPGTA

Important features:

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 1039-1064

N-glycosylation sites.

amino acids 86-89, 746-749, 949-952, 985-988 and 1005-1008

Integrins alpha chain proteins.

amino acids 1064-1071, 384-408, 1041-1071, 317-346, 443-465, 385-407, 215-224, 634-647, 85-99, 322-346, 470-479, 442-466, 379-408 and 1031-1047

AAGCAGCGAGTTGGCAGAGCAGGGCTGCATTTCCAGCAGGAGCTGCGAGCACAGTGCTGGCT TGGATGATAAACAATGGCTCACCACAATCTCTCAGTATGACAAGGAAGTCGGACAGTGGAAC AAATTCCGAGACGAAGTAGAGGATGATTATTTCCGCACTTGGAGTCCAGGAAAACCCTTCGA TCAGGCTTTAGATCCAGCTAAGGATCCATGCTTAAAGATGAAATGTAGTCGCCATAAAGTAT GCATTGCTCAAGATTCTCAGACTGCAGTCTGCATTAGTCACCGGAGGCTTACACACAGGATG AAAGAAGCAGGAGTAGACCATAGGCAGTGGAGGGGTCCCATATTATCCACCTGCAAGCAGTG CCCAGTGGTCTATCCCAGCCCTGTTTGTGGTTCAGATGGTCATACCTACTCTTTTCAGTGCA **AACTAGAATATCAGGCATGTGTCTTAGGAAAACAGATCTCAGTCAAATGTGAAGGACATTGC** CCATGTCCTTCAGATAAGCCCACCAGTACAAGCAGAAATGTTAAGAGAGCATGCAGTGACCT GGAGTTCAGGGAAGTGGCAAACAGATTGCGGGACTGGTTCAAGGCCCTTCATGAAAGTGGAA GTCAAAACAAGAAGACAAAAACATTGCTGAGGCCTGAGAGAAGCAGATTCGATACCAGCATC TTGCCAATTTGCAAGGACTCACTTGGCTGGATGTTTAACAGACTTGATACAAACTATGACCT GCTATTGGACCAGTCAGAGCTCAGAAGCATTTACCTTGATAAGAATGAACAGTGTACCAAGG CATTCTTCAATTCTTGTGACACATACAAGGACAGTTTAATATCTAATAATGAGTGGTGCTAC TGCTTCCAGAGACAGCAAGACCCACCTTGCCAGACTGAGCTCAGCAATATTCAGAAGCGGCA **AGGGGTAAAGAAGCTCCTAGGACAGTATATCCCCCTGTGTGATGAAGATGGTTACTACAAGC** CAACACAATGTCATGGCAGTGTTGGACAGTGCTGGTGTTGACAGATATGGAAATGAAGTC ATGGGATCCAGAATAAATGGTGTTGCAGATTGTGCTATAGATTTTGAGATCTCCGGAGATTT TGCTAGTGGCGATTTTCATGAATGGACTGATGATGAGGGTGATGAAGACGATATTATGAATG CATGATGTATACATT<u>TGA</u>TTGATGACAGTTGAAATCAATAAATTCTACATTTCTAATATTTA CAAAAATGATAGCCTATTTAAAATTATCTTCTTCCCCAATAACAAAATGATTCTAAACCTCA CATATATTTTGTATAATTATTTGAAAAATTGCAGCTAAAGTTATAGAACTTTATGTTTAAAT **AAGAATCATTTGCTTTGAGTTTTTATATTCCTTACACAAAAAGAAAATACATATGCAGTCTA** GTCAGACAAAATAAAGTTTTGAAGTGCTACTATAATAAATTTTTCACGAGAACAAACTTTGT **AAATCTTCCATAAGCAAAATGACAGCTAGTGCTTGGGATCGTACATGTTAATTTTTTGAAAG** ATAATTCTAAGTGAAATTAAAATAAATAAATTTTTTAATGACCTGGGTCTTAAGGATTTAGG AAAAATATGCATGCTTTAATTGCATTTCCAAAGTAGCATCTTGCTAGACCTAGATGAGTCAG

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49829

><subunit 1 of 1, 436 aa, 1 stop

><MW: 49429, pI: 4.80, NX(S/T): 0

MLKVSAVLCVCAAAWCSQSLAAAAAVAAAGGRSDGGNFLDDKQWLTTISQYDKEVGQWNKFR
DEVEDDYFRTWSPGKPFDQALDPAKDPCLKMKCSRHKVCIAQDSQTAVCISHRRLTHRMKEA
GVDHRQWRGPILSTCKQCPVVYPSPVCGSDGHTYSFQCKLEYQACVLGKQISVKCEGHCPCP
SDKPTSTSRNVKRACSDLEFREVANRLRDWFKALHESGSQNKKTKTLLRPERSRFDTSILPI
CKDSLGWMFNRLDTNYDLLLDQSELRSIYLDKNEQCTKAFFNSCDTYKDSLISNNEWCYCFQ
RQQDPPCQTELSNIQKRQGVKKLLGQYIPLCDEDGYYKPTQCHGSVGQCWCVDRYGNEVMGS
RINGVADCAIDFEISGDFASGDFHEWTDDEDDEDDIMNDEDEIEDDDEDGDDDDGGDDHDVYI

Important features:

Signal peptide:

amino acids 1-16

Leucine zipper pattern.

amino acids 246-267

N-myristoylation sites.

amino acids 357-362, 371-376 and 376-381

Thyroglobulin type-1 repeat proteins

amino acids 353-365 and 339-352

FIGURE 180A

CAGACTCCAGATTTCCCTGTCAACCACGAGGGGGTCCAGAGAGGGAAACGCGGAGCGGAGACAA CAGTACCTGACGCCTCTTTCAGCCCGGGATCGCCCCAGCAGGGGATCGGCGACAAGATCTGGC TTCACACCTTCCCTCGATAGCGACTTCACCTTTACCCTTCCCGCCGGCCAGAAGGAGTGCTT CTACCAGCCCATGCCCCTGAAGGCCTCGCTGGAGATCGAGTACCAAGTTTTAGATGGAGCAG GATTAGATATTGATTTCCATCTTGCCTCTCCAGAAGGCAAAACCTTAGTTTTTGAACAAAGA AAATCAGATGGAGTTCACACTGTAGAGACTGAAGTTGGTGATTACATGTTCTGCTTTGACAA TACATTCAGCACCATTTCTGAGAAGGTGATTTTCTTTGAATTAATCCTGGATAATATGGGAG **AACAGGCACAAGAACAAGAAGATTGGAAGAAATATATTACTGGCACAGATATATTGGATATG** AAACTGGAAGACATCCTGGAATCCATCAACAGCATCAAGTCCAGACTAAGCAAAAGTGGGCA CATACAAATTCTGCTTAGAGCATTTGAAGCTCGTGATCGAAACATACAAGAAAGCAACTTTG ATAGAGTCAATTTCTGGTCTATGGTTAATTTAGTGGTCATGGTGGTGGTCAGCCATTCAA GTTTATATGCTGAAGAGTCTGTTTGAAGATAAGAGGAAAAGTAGAACT AGAGTACGTAACATTGAAAAATGAGGCATAAAAATGCAATAAACTGTTACAGTCAAGACCAT TAATGGTCTTCTCCAAAATATTTTGAGATATAAAAGTAGGAAACAGGTATAATTTTAATGTG AAAATTAAGTCTTCACTTTCTGTGCAAGTAATCCTGCTGATCCAGTTGTACTTAAGTGTGTA ACAGGAATATTTGCAGAATATAGGTTTAACTGAATGAAGCCATATTAATAACTGCATTTTC TGCAACACCAGTCTGTTTTTAACAGGTTCTATTACCCAGAACTTTTTTGTAAATGCGGCAGT TACAAATTAACTGTGGAAGTTTTCAGTTTTAAGTTATAAATCACCTGAGAATTACCTAATGA TGGATTGAATAAATCTTTAGACTACAAAAGCCCAACTTTTCTCTATTTACATATGCATCTCT CCTATAATGTAAATAGAATAATAGCTTTGAAATACAATTAGGTTTTTGAGATTTTTATAACC AAATACATTTCAGTGTAACATATTAGCAGAAAGCATTAGTCTTTGTACTTTGCTTACATTCC CAAAAGCTGACATTTTCACGATTCTTAAAAACACAAAGTTACACTTACTAAAATTAGGACAT GTTTTCTCTTTGAAATGAAGAATATAGTTTAAAAGCTTCCTCCTCCATAGGGACACATTTTC TCTAACCCTTAACTAAAGTGTAGGATTTTAAAATTAAATGTGAGGTAAAATAAGTTTATTTT TAATAGTATCTGTCAAGTTAATATCTGTCAACAGTTAATAATCATGTTATGTTAATTTTAAC ATGATTGCTGACTTGGATAATTCATTATTACCAGCAGTTATGAAGGAAATATTGCTAAAATG ATCTGGGCCTACCATAAATAAATATCTCCTTTTCTGAGCTCTAAGAATTATCAGAAAACAGG AAAGAATTTAGAAAAACTTGAGAAAACCTAATCCAAAATAAAATTCACTTAAGTAGAACTAT **AAATAAATATCTAGAATCTGACTGGCTCATCATGACATCCTACTCATAACATAAATCAAAGG** AGATGATTAATTTCCAGTTAGCTGGAAGAACTTTGGCTGTAGGTTTTTATTTTCTACAAGA ATTCTGGTTTGAATTATTTTTGTAAGCAGGTACATTTTATAAAATGTAAGCCCTACTGTAAG CCTTTCTGAACACTTTATTTATTGATGTTGAAGTAAGGATTAGAAACATAGACTCCCAAGTT TTAAACACCTAAATGTGAATAACCCATATATACAACAAAGTTTCTGCCATCTAGCTTTTTGA ATTTGGGGTATAGAACCCCTCAACAGGTTAGTAATGCTGGAATTCTTGATGAGCAATAATGA TAACCAGAGAGTGATTTCATTTACACTCATAGTAGTATAAAAAGAGATACATTTCCCTCTTA GGCCCCTGGGAGAAGAGCAGCTTAGATTTCCCTACTGGCAAGGTTTTTAAAAATGAGGTAAA TGCCGTATATGATCAATTACCTTAATTGGCCAAGAAAATGCTTCAGGTGTCTAGGGGTATCC CGCTGTTAAATTTGCAATGAGAAGCAAATTTACAGTACCATAACTAATAAAGCAGGGTACAG ATATAAACTACTGCATCTTTTCTATAAAACTGTGATTAAGAATTCTACCTCTCCTGTATGGC TGTTACTGTACTGTACTCTGACTCCTTACCTAACAATGAATTTGTTACATAATCTTCTAC ATGTATGATTTGTGCCACTGATCTTAAACCTATGATTCAGTAACTTCTTACCATATAAAAAC GATAATTGCTTTATTTGGAAAAGAATTTAGGAATACTAAGGACAATTATTTTTATAGACAAA GTAAAAAGACAGATATTTAAGAGGCATAACCAAAAAAGCAAAACTTGTAAACAGAGTAAAAA TCTTTAATATTTCTAAAGACATACTGTTTATCTGCTTCATATGCTTTTTTTAATTTCACTAT TCCATTTCTAAATTAAAGTTATGCTAAATTGAGTAAGCTGTTTATCACTTAACAGCTCATTT TGTCTTTTTCAATATACAAATTTTAAAAATACTACAATATTTAACTAAGGCCCAACCGATTT CCATAATGTAGCAGTTACCGTGTTCACCTCACACTAAGGCCTAGAGTTTGCTCTGATATGCA TTTGGATGATTAATGTTATGCTGTTCTTTCATGTGAATGTCAAGACATGGAGGGTGTTTGTA

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FIGURE 180B

ATTTTATGGTAAAATTAATCCTTCTTACACATAATGGTGTCTTAAAATTGACAAAAAATGAG CACTTACAATTGATGTCTCCTCAAATGAAGATTCTTTATGTGAAATTTTAAAAGACATTGA TTCCGCATGTAAGGATTTTTCATCTGAAGTACAAATAATGCACAATCAGTGTTGCTCAAACTG CTTTATACTTATAAACAGCCATCTTAAATAAGCAACGTATTGTGAGTACTGATATGTATATA ATAAAAATTATCAAAGGAAAA

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FIGURE 181

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA52196

><subunit 1 of 1, 229 aa, 1 stop

><MW: 26017, pI: 4.73, NX(S/T): 0

MGDKIWLPFPVLLLAALPPVLLPGAAGFTPSLDSDFTFTLPAGQKECFYQPMPLKASLEIEY QVLDGAGLDIDFHLASPEGKTLVFEQRKSDGVHTVETEVGDYMFCFDNTFSTISEKVIFFEL ILDNMGEQAQEQEDWKKYITGTDILDMKLEDILESINSIKSRLSKSGHIQILLRAFEARDRN IQESNFDRVNFWSMVNLVVMVVVSAIQVYMLKSLFEDKRKSRT

Important features:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 195-217

N-myristoylation site.

amino acids 43-48

Tyrosine kinase phosphorylation site.

amino acids 55-62

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FIGURE 183

</usr/segdb2/sst/DNA/Dnaseqs.min/ss.DNA56965</pre>

<subunit 1 of 1, 175 aa, 1 stop

<MW: 19330, pI: 7.25, NX(S/T): 1

MLPPMALPSVSWMLLSCLILLCQVQGEETQKELPSPRISCPKGSKAYGSPCYALFLSPKSWM DADLACQKRPSGKLVSVLSGAEGSFVSSLVRSISNSYSYIWIGLHDPTQGSEPDGDGWEWSS TDVMNYFAWEKNPSTILNPGHCGSLSRSTGFLKWKDYNCDAKLPYVCKFKD

Important features:

Signal peptide:

amino acids 1-26

C-type lectin domain signature.

amino acids 146-171



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FIGURE 185

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56405</pre>

<subunit 1 of 1, 125 aa, 1 stop

<MW: 13115, pI: 5.90, NX(S/T): 1

MRGTRLALLALVLAACGELAPALRCYVCPEPTGVSDCVTIATCTTNETMCKTTLYSREIVYP FQGDSTVTKSCASKCKPSDVDGIGQTLPVSCCNTELCNVDGAPALNSLHCGALTLLPLLSLRL

Important features:

Signal peptide:

amino acids 1-17

N-glycosylation site.

amino acids 46-49

CTGCAGTCAGGACTCTGGGACCGCAGGGGGCTCCCGGACCCTGACTCTGCAGCCGAACCGGC ${\tt GAG}{\tt TCCTTCTGAG}{\tt ATG}{\tt ATG}{\tt GCTCTGGGCGCAGCGGGAGCTACCCGGGTCTTTGTCGCGATGG}$ TAGCGGCGGCTCTCGGCGGCCACCTCTGCTGGGAGTGAGCGCCACCTTGAACTCGGTTCTC TGCAGTCAGCGCCGCGGGAATCCTGTACCCGGGCGGGAATAAGTACCAGACCATTGACA ACTACCAGCCGTACCCGTGCGCAGAGGACGAGGAGTGCGCACTGATGAGTACTGCGCTAGT CCCACCCGCGGAGGGGACGCAGGCGTGCAAATCTGTCTCGCCTGCAGGAAGCGCCGAAAACG CTGCATGCGTCACGCTATGTGCTGCCCCGGGAATTACTGCAAAAATGGAATATGTGTGTCTT CTGATCAAAATCATTTCCGAGGAGAAATTGAGGAAACCATCACTGAAAGCTTTGGTAATGAT CATAGCACCTTGGATGGGTATTCCAGAAGAACCACCTTGTCTTCAAAAATGTATCACACCAA AGGACAAGAAGGTTCTGTTTGTCTCCGGTCATCAGACTGTGCCTCAGGATTGTGTTGTGCTA GACACTTCTGGTCCAAGATCTGTAAACCTGTCCTGAAAGAAGGTCAAGTGTGTACCAAGCAT AGGAGAAAAGGCTCTCATGGACTAGAAATATTCCAGCGTTGTTACTGTGGAGAAGGTCTGTC TTGCCGGATACAGAAAGATCACCATCAAGCCAGTAATTCTTCTAGGCTTCACACTTGTCAGA GACACTAAACCAGCTATCCAAATGCAGTGAACTCCTTTTATATAATAGATGCTATGAAAACC TTTTATGACCTTCATCAACTCAATCCTAAGGATATACAAGTTCTGTGGTTTCAGTTAAGCAT TCCAATAACACCTTCCAAAAACCTGGAGTGTAAGAGCTTTGTTTCTTTATGGAACTCCCCTG TGATTGCAGTAAATTACTGTATTGTAAATTCTCAGTGTGGCACTTACCTGTAAATGCAATGA AACTTTTAATTATTTTTCTAAAGGTGCTGCACTGCCTATTTTTCCTCTTGTTATGTAAATTT TTGTACACATTGATTGTTATCTTGACTGACAAATATTCTATATTGAACTGAAGTAAATCATT TCAGCTTATAGTTCTTAAAAGCATAACCCTTTACCCCATTTAATTCTAGAGTCTAGAACGCA AGGATCTCTTGGAATGACAAATGATAGGTACCTAAAATGTAACATGAAAATACTAGCTTATT TTCTGAAATGTACTATCTTAATGCTTAAATTATATTTCCCTTTAGGCTGTGATAGTTTTTGA AATAAAATTTAACATTTAAAAAAAAAAAAA

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57530

<subunit 1 of 1, 266 aa, 1 stop

<MW: 28672, pI: 8.85, NX(S/T): 1

MMALGAAGATRVFVAMVAAALGGHPLLGVSATLNSVLNSNAIKNLPPPLGGAAGHPGSAVSA APGILYPGGNKYQTIDNYQPYPCAEDEECGTDEYCASPTRGGDAGVQICLACRKRRKRCMRH AMCCPGNYCKNGICVSSDQNHFRGEIEETITESFGNDHSTLDGYSRRTTLSSKMYHTKGQEG SVCLRSSDCASGLCCARHFWSKICKPVLKEGQVCTKHRRKGSHGLEIFQRCYCGEGLSCRIQ KDHHQASNSSRLHTCQRH

Important features:

Signal peptide:

amino acids 1-23

N-glycosylation site.

amino acids 256-259

Fungal Zn(2)-Cys(6) binuclear cluster domain amino acids 110-126

FIGURE 189A

GAGGAACCTACCGGTACCGGCGCGCGCGGTGTAGTCGCCGGTGTGGCTGCACCTCACCAATC GCTCGGCCAGGGTCCGCCGCCAGGGTTTGAGGATGGGGGAGTAGCTACAGGAAGCGAC CCCGCGATGGCAAGGTATATTTTTGTGGAATGAAAAGGAAGTATTAGAAATGAGCTGAAGAC CATTCACAGATTAATATTTTTGGGGACAGATTTGTGATGCTTGATTCACCCTTGAAGTAATG TAGACAGAAGTTCTCAAATTTGCATATTACATCAACTGGAACCAGCAGTGAATCTTAATGTT CACTTAAATCAGAACTTGCATAAGAAAGAGAGA<mark>ATG</mark>GGAGTCTGGTTAAATAAAGATGACTATA TCAGAGACTTGAAAAGGATCATTCTCTGTTTTCTGATAGTGTATATGGCCATTTTAGTGGGC ACAGATCAGGATTTTTACAGTTTACTTGGAGTGTCCAAAACTGCAAGCAGTAGAGAAATAAG ACAAGCTTTCAAGAAATTGGCATTGAAGTTACATCCTGATAAAAACCCGAATAACCCAAATG CACATGGCGATTTTTTAAAAATAAATAGAGCATATGAAGTACTCAAAGATGAAGATCTACGG AAAAAGTATGACAAATATGGAGAAAAGGGACTTGAGGATAATCAAGGTGGCCAGTATGAAAG CTGGAACTATTATCGTTATGATTTTGGTATTTATGATGATGATCCTGAAATCATAACATTGG AAAGAAGAGAATTTGATGCTGCTGTTAATTCTGGAGAACTGTGGTTTGTAAATTTTTACTCC CCAGGCTGTTCACACTGCCATGATTTAGCTCCCACATGGAGAGACTTTGCTAAAGAAGTGGA TGGGTTACTTCGAATTGGAGCTGTTAACTGTGGTGATGATAGAATGCTTTGCCGAATGAAAG GAGTCAACAGCTATCCCAGTCTCTTCATTTTTCGGTCTGGAATGGCCCCAGTGAAATATCAT GGAGACAGATCAAAGGAGAGTTTAGTGAGTTTTGCAATGCAGCATGTTAGAAGTACAGTGAC AGAACTTTGGACAGGAAATTTTGTCAACTCCATACAAACTGCTTTTGCTGCTGGTATTGGCT GGCTGATCACTTTTTGTTCAAAAGGAGGAGATTGTTTGACTTCACAGACACGACTCAGGCTT AGTGGCATGTTGTTTCTCAACTCATTGGATGCTAAAGAAATATATTTGGAAGTAATACATAA TCTTCCAGATTTTGAACTACTTTCGGCAAACACACTAGAGGATCGTTTGGCTCATCATCGGT GGCTGTTATTTTTCATTTTGGAAAAATGAAAATTCAAATGATCCTGAGCTGAAAAAACTA AAAACTCTACTTAAAAATGATCATATTCAAGTTGGCAGGTTTGACTGTTCCTCTGCACCAGA CATCTGTAGTAATCTGTATGTTTTTCAGCCGTCTCTAGCAGTATTTAAAGGACAAGGAACCA AAGAATATGAAATTCATCATGGAAAGAAGATTCTATATGATATACTTGCCTTTGCCAAAGAA AGTGTGAATTCTCATGTTACCACGCTTGGACCTCAAAATTTTCCTGCCAATGACAAAGAACC ATGGCTTGTTGATTTCTTTGCCCCCTGGTGTCCACCATGTCGAGCTTTACTACCAGAGTTAC GAAGAGCATCAAATCTTCTTTATGGTCAGCTTAAGTTTGGTACACTAGATTGTACAGTTCAT GAGGGACTCTGTAACATGTATAACATTCAGGCTTATCCAACAACAGTGGTATTCAACCAGTC CAACATTCATGAGTATGAAGGACATCACTCTGCTGAACAAATCTTGGAGTTCATAGAGGATC TTATGAATCCTTCAGTGGTCTCCCTTACACCCACCACCTTCAACGAACTAGTTACACAAAGA AAACACAACGAAGTCTGGATGGTTGATTTCTATTCTCCGTGGTGTCATCCTTGCCAAGTCTT AATGCCAGAATGGAAAAGAATGGCCCGGACATTAACTGGACTGATCAACGTGGGCAGTATAG ATTGCCAACAGTATCATTCTTTTTGTGCCCAGGAAAACGTTCAAAGATACCCTGAGATAAGA TTTTTTCCCCCAAAATCAAATAAAGCTTATCAGTATCACAGTTACAATGGTTGGAATAGGGA TGCTTATTCCCTGAGAATCTGGGGTCTAGGATTTTTACCTCAAGTATCCACAGATCTAACAC CCTTGGTGTGGACCTTGCCAGAATTTTGCTCCAGAATTTGAGCTCTTGGCTAGGATGATTAA AGGAAAAGTGAAAAGTAGACTGTCAGGCTTATGCTCAGACATGCCAGAAAGCTG GGATCAGGGCCTATCCAACTGTTAAGTTTTATTTCTACGAAAGAGCAAAGAGAAATTTTCAA GAAGAGCAGATAAATACCAGAGATGCAAAAGCAATCGCTGCCTTAATAAGTGAAAAATTGGA AACTCTCCGAAATCAAGGCAAGAGGAATAAGGATGAACTT<u>TGA</u>TAATGTTGAAGATGAAGAA AAAGTTTAAAAGAAATTCTGACAGATGACATCAGAAGACACCTATTTAGAATGTTACATTTA TGATGGGAATGAACATTATCTTAGACTTGCAGTTGTACTGCCAGAATTATCTACAGCA CTGGTGTAAAAGAAGGTCTGCAAACTTTTTCTGTAAAGGGCCGGTTTATAAATATTTTAGA CTTTGCAGGCTATAATATATGGTTCACACATGAGAACAAGAATAGAGTCATCATGTATTCTT TGTTATTTGCTTTTAACAACCTTTAAAAAATATTAAAACGATTCTTAGCTCAGAGCCATACA AAAGTAGGCTGGATTCAGTCCATGGACCATAGATTGCTGTCCCCCTCGACGGACTTATAATG TTTCAGGTGGCTGGCTTGAACATGAGTCTGCTGTGCTATCTACATAAATGTCTAAGTTGTAT AAAGTCCACTTTCCCTTCACGTTTTTTGGCTGACCTGAAAAGAGGGTAACTTAGTTTTTGGTC ACTTGTTCTCCTAAAAATGCTATCCCTAACCATATATTTATATTTCGTTTTAAAAAACACCCA TGATGTGGCACAGTAAACAAACCCTGTTATGCTGTATTATTATGAGGAGATTCTTCATTGTT TTCTTTCCTTCTCAAAGGTTGAAAAAATGCTTTTAATTTTTCACAGCCGAGAAACAGTGCAG

FIGURE 189B

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56439</pre>

<subunit 1 of 1, 747 aa, 1 stop

<MW: 86127, pI: 7.46, NX(S/T): 2

MGVWLNKDDYIRDLKRIILCFLIVYMAILVGTDQDFYSLLGVSKTASSREIRQAFKKLALKL
HPDKNPNNPNAHGDFLKINRAYEVLKDEDLRKKYDKYGEKGLEDNQGGQYESWNYYRYDFGI
YDDDPEIITLERREFDAAVNSGELWFVNFYSPGCSHCHDLAPTWRDFAKEVDGLLRIGAVNC
GDDRMLCRMKGVNSYPSLFIFRSGMAPVKYHGDRSKESLVSFAMQHVRSTVTELWTGNFVNS
IQTAFAAGIGWLITFCSKGGDCLTSQTRLRLSGMLFLNSLDAKEIYLEVIHNLPDFELLSAN
TLEDRLAHHRWLLFFHFGKNENSNDPELKKLKTLLKNDHIQVGRFDCSSAPDICSNLYVFQP
SLAVFKGQGTKEYEIHHGKKILYDILAFAKESVNSHVTTLGPQNFPANDKEPWLVDFFAPWC
PPCRALLPELRRASNLLYGQLKFGTLDCTVHEGLCNMYNIQAYPTTVVFNQSNIHEYEGHHS
AEQILEFIEDLMNPSVVSLTPTTFNELVTQRKHNEVWMVDFYSPWCHPCQVLMPEWKRMART
LTGLINVGSIDCQQYHSFCAQENVQRYPEIRFFPPKSNKAYQYHSYNGWNRDAYSLRIWGLG
FLPQVSTDLTPQTFSEKVLQGKNHWVIDFYAPWCGPCQNFAPEFELLARMIKGKVKAGKVDC
QAYAQTCQKAGIRAYPTVKFYFYERAKRNFQEEQINTRDAKAIAALISEKLETLRNQGKRNKDEL

Important features:

Endoplasmic reticulum targeting sequence.

amino acids 744-747

Cytochrome c family heme-binding site signature.

amino acids 158-163

Nt-dnaJ domain signature.

amino acids 77-96

N-glycosylation site.

amino acids 484-487

GCC<u>ATG</u>AACATCATCCTAGAAATCCTTCTGCTTCTGATCACCATCATCTACTCCTACTTGGA GTCGTTGGTGAAGTTTTTCATTCCTCAGAGGAGAAAATCTGTGGCTGGGGAGATTGTTCTCA TTACTGGAGCTGGGCATGGAATAGGCAGGCAGACTACTTATGAATTTGCAAAACGACAGAGC ATATTGGTTCTGTGGGATATTAATAAGCGCGGTGTGGAGGAAACTGCAGCTGAGTGCCGAAA ACTAGGCGTCACTGCGCATGCGTATGTGGTAGACTGCAGCAACAGAGAAGAGATCTATCGCT CTCTAAATCAGGTGAAGAAGAAGTGGGTGATGTAACAATCGTGGTGAATAATGCTGGGACA GTATATCCAGCCGATCTTCTCAGCACCAAGGATGAAGAGATTACCAAGACATTTGAGGTCAA CATCCTAGGACATTTTTGGATCACAAAAGCACTTCTTCCATCGATGATGGAGAGAAATCATG GCCACATCGTCACAGTGGCTTCAGTGTGCGGCCACGAAGGGATTCCTTACCTCATCCCATAT TGTTCCAGCAAATTTGCCGCTGTTGGCTTTCACAGAGGTCTGACATCAGAACTTCAGGCCTT GGGAAAAACTGGTATCAAAACCTCATGTCTCTGCCCAGTTTTTGTGAATACTGGGTTCACCA AAAATCCAAGCACAAGATTATGGCCTGTATTGGAGACAGATGAAGTCGTAAGAAGTCTGATA GATGGAATACTTACCAATAAGAAAATGATTTTTGTTCCATCGTATATCAATATCTTTCTGAG ACTACAGAAGTTTCTTCCTGAACGCGCCTCAGCGATTTTAAATCGTATGCAGAATATTCAAT TTGAAGCAGTGGTTGGCCACAAAATCAAAATGAAA<u>TGA</u>ATAAATAAGCTCCAGCCAGAGATG TATGCATGATAATGATATGAATAGTTTCGAATCAATGCTGCAAAGCTTTATTTCACATTTTT TCAGTCCTGATAATATTAAAAACATTGGTTTGGCACTAGCAGCAGTCAAACGAACAAGATTA ATTACCTGTCTTCCTGTTTCTCAAGAATATTTACGTAGTTTTTCATAGGTCTGTTTTTCCTT TCATGCCTCTTAAAAACTTCTGTGCTTACATAAACATACTTAAAAGGTTTTCTTTAAGATAT TTTATTTTTCCATTTAAAGGTGGACAAAAGCTACCTCCCTAAAAGTAAATACAAAGAGAACT TATTTACACAGGGAAGGTTTAAGACTGTTCAAGTAGCATTCCAATCTGTAGCCATGCCACAG ATCTCAACCTGGACATATTTTAAGATTCAGCATTTGAAAGATTTCCCTAGCCTCTTCCTTTT TCATTAGCCCAAAACGGTGCAACTCTATTCTGGACTTTATTACTTGATTCTGTCTTGTAT AACTCTGAAGTCCACCAAAAGTGGACCCTCTATATTTCCTCCCTTTTTATAGTCTTATAAGA TACATTATGAAAGGTGACCGACTCTATTTTAAATCTCAGAATTTTAAGTTCTAGCCCCATGA TAACCTTTTTCTTTGTAATTTATGCTTTCATATATCCTTGGTCCCAGAGATGTTTAGACAAT TTTAGGCTCAAAAATTAAAGCTAACACAGGAAAAGGAACTGTACTGGCTATTACATAAGAAA CAATGGACCCAAGAGAAGAA

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56409</pre>

<subunit 1 of 1, 300 aa, 1 stop

<MW: 33655, pI: 9.31, NX(S/T): 1

MNIILEILLLITIIYSYLESLVKFFIPQRRKSVAGEIVLITGAGHGIGRQTTYEFAKRQSI LVLWDINKRGVEETAAECRKLGVTAHAYVVDCSNREEIYRSLNQVKKEVGDVTIVVNNAGTV YPADLLSTKDEEITKTFEVNILGHFWITKALLPSMMERNHGHIVTVASVCGHEGIPYLIPYC SSKFAAVGFHRGLTSELQALGKTGIKTSCLCPVFVNTGFTKNPSTRLWPVLETDEVVRSLID GILTNKKMIFVPSYINIFLRLQKFLPERASAILNRMQNIQFEAVVGHKIKMK

Important features:

Signal peptide:

amino acids 1-19

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 30-33 and 58-61

Short-chain alcohol dehydrogenase family protein amino acids 165-202, 37-49, 112-122 and 210-219

CGGCGGCGGCGGGGCGAGGTGAGGGGCGCGAGGTTCCCAGCAGG ${\tt AGG} \underline{\textbf{ATG}} \\ {\tt ACCAAGGCCCGGCTGTTCCGGCTGTGGCTGGTGCTGGGGTCGGTGTTCATGATCCT} \\$ GCTGATCATCGTGTACTGGGACAGCGCAGGCGCGCGCGCACTTCTACTTGCACACGTCCTTCT CTAGGCCGCACACGGGCCGCCGCCCCACGCCCGGGCCGGACAGGGACAGGGAGCTCACG GCCGACTCCGATGTCGACGAGTTTCTGGACAAGTTTCTCAGTGCTGGCGTGAAGCAGAGCGA CCTTCCCAGAAAGGAGACGGAGCAGCCGCCTGCGCCGGGGAGCATGGAGAGCGTGAGAG CGGAGGAGCGTGCTGCGGGGCTTCTGCGCCAACTCCAGCCTGGCCTTCCCCACCAAGGAGCG CGCATTCGACGACATCCCCAACTCGGAGCTGAGCCACCTGATCGTGGACGACCGGCACGGGG CCATCTACTGCTACGTGCCCAAGGTGGCCTGCACCAACTGGAAGCGCGTGATGATCGTGCTG AGCGGAAGCCTGCTGCACCGCGGTGCGCCCTACCGCGACCCGCTGCGCATCCCGCGCGAGCA CGTGCACAACGCCAGCGCGCACCTGACCTTCAACAAGTTCTGGCGCCGCTACGGGAAGCTCT CCCGCCACCTCATGAAGGTCAAGCTCAAGAAGTACACCAAGTTCCTCTTCGTGCGCGACCCC TTCGTGCGCCTGATCTCCGCCTTCCGCAGCAAGTTCGAGCTGGAGAACGAGGAGTTCTACCG CAAGTTCGCCGTGCCCATGCTGCGGCTGTACGCCAACCACCAGCCTGCCCGCCTCGGCGC GCGAGGCCTTCCGCGCTGGCCTCAAGGTGTCCTTCGCCAACTTCATCCAGTACCTGCTGGAC CCGCACACGGAGAAGCTGGCGCCCTTCAACGAGCACTGGCGGCAGGTGTACCGCCTCTGCCA CCCGTGCCAGATCGACTACGACTTCGTGGGGGAAGCTGGAGACTCTGGACGAGGACGCCGCGC AGCTGCTGCAGCTACTCCAGGTGGACCGGCAGCTCCGCTTCCCCCGAGCTACCGGAACAGG ACCGCCAGCAGCTGGGAGGAGGACTGGTTCGCCAAGATCCCCCTGGCCTGGAGGCAGCAGCT GTATAAACTCTACGAGGCCGACTTTGTTCTCTTCGGCTACCCCAAGCCCGAAAACCTCCTCC AGTTTTTTTATGACCTACGATTTTGCAATCTGGGCTTCTTGTTCACTCCACTGCCTCTATCC ATTGAGTACTGTATCGATATTGTTTTTTAAGATTAATATTTCAGGTATTTAATACGA

WO 99/46281 PCT/US99/05028

FIGURE 194

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56112</pre>

<subunit 1 of 1, 414 aa, 1 stop

<MW: 48414, pI: 9.54, NX(S/T): 4

MTKARLFRLWLVLGSVFMILLIIVYWDSAGAAHFYLHTSFSRPHTGPPLPTPGPDRDRELTA
DSDVDEFLDKFLSAGVKQSDLPRKETEQPPAPGSMEESVRGYDWSPRDARRSPDQGRQQAER
RSVLRGFCANSSLAFPTKERAFDDIPNSELSHLIVDDRHGAIYCYVPKVACTNWKRVMIVLS
GSLLHRGAPYRDPLRIPREHVHNASAHLTFNKFWRRYGKLSRHLMKVKLKKYTKFLFVRDPF
VRLISAFRSKFELENEEFYRKFAVPMLRLYANHTSLPASAREAFRAGLKVSFANFIQYLLDP
HTEKLAPFNEHWRQVYRLCHPCQIDYDFVGKLETLDEDAAQLLQLLQVDRQLRFPPSYRNRT
ASSWEEDWFAKIPLAWRQQLYKLYEADFVLFGYPKPENLLRD

Important features:

Signal peptide:

amino acids 1-31

N-glycosylation sites.

amino acids 134-137, 209-212, 280-283 and 370-373

TNFR/NGFR family cysteine-rich region protein amino acids 329-332



TCGGGCCAGAATTCGGCACGAGGCGCACGAGGGCGACGGCCTCACGGGGCTTTGGAGGTGA AAGAGGCCCAGAGTAGAGAGAGAGAGAGACCGACGTACACGGGA<u>ATG</u>GCTACGGGAACGCGCT GCCTTCGTGAACAGCGGGGCCCGAGTGGTTATCTGCGACAAGGATGAGTCTGGGGGCCGGGC CCTGGAGCAGGAGCTCCCTGGAGCTGTCTTTATCCTCTGTGATGTGACTCAGGAAGATGATG TGAAGACCCTGGTTTCTGAGACCATCCGCCGATTTGGCCGCCTGGATTGTGTCTCAACAAC GCTGGCCACCACCCCCACAGAGGCCTGAGGAGACCTCTGCCCAGGGATTCCGCCAGCT GCTGGAGCTGAACCTACTGGGGACGTACACCTTGACCAAGCTCGCCCTACCTGCGGA AGAGTCAAGGGAATGTCATCAACATCTCCAGCCTGGTGGGGGCAATCGGCCAGGCCCAGGCA GTTCCCTATGTGGCCACCAAGGGGGCAGTAACAGCCATGACCAAAGCTTTGGCCCTGGATGA AAGTCCATATGGTGTCCGAGTCAACTGTATCTCCCCAGGAAACATCTGGACCCCGCTGTGGG AGGAGCTGGCAGCCTTAATGCCAGACCCTAGGGCCACAATCCGAGAGGGCATGCTGGCCCAG CCACTGGGCCGCATGGGCCCAGCCCGCTGAGGTCGGGCTGCGGCAGTGTTCCTGGCCTCCGA ${\tt AGCCAACTTCTGCACGGGCATTGAACTGCTCGTGACGGGGTGCAGAGCTGGGGTACGGGT}$ ${\tt GCAAGGCCAGTCGGAGCACCCCCGTGGACGCCCCCGATATCCCTTCC} \underline{{\tt TGA}}{\tt TTTCTCTCATTT}$ CTACTTGGGGCCCCCTTCCTAGGACTCTCCCACCCCAAACTCCAACCTGTATCAGATGCAGC $\tt CCCCAAGCCCTTAGACTCTAAGCCCAGTTAGCAAGGTGCCGGGTCACCCTGCAGGTTCCCAT$ AAAAACGATTTGCAGCC

WO 99/46281 PCT/US99/05028

FIGURE 196

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56045
<subunit 1 of 1, 270 aa, 1 stop
<MW: 28317, pI: 6.00, NX(S/T): 1

MATGTRYAGKVVVVTGGGRGIGAGIVRAFVNSGARVVICDKDESGGRALEQELPGAVFILCD
VTQEDDVKTLVSETIRRFGRLDCVVNNAGHHPPPQRPEETSAQGFRQLLELNLLGTYTLTKL
ALPYLRKSQGNVINISSLVGAIGQAQAVPYVATKGAVTAMTKALALDESPYGVRVNCISPGN
IWTPLWEELAALMPDPRATIREGMLAQPLGRMGQPAEVGAAAVFLASEANFCTGIELLVTGG</pre>

Important features:

N-glycosylation site.

AELGYGCKASRSTPVDAPDIPS

amino acids 138-141

Short-chain alcohol dehydrogenase family protein amino acids 10-22, 81-91, 134-171 and 176-185



AGGCGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGAATGGACTGGCCTCACAACCTG
CTGTTTCTTCTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAA
GAGGAAGGGGCAAGGGCGGCCTGGGCCCTGGCCCCTGGCCCTCACCAGGTGCCACTGGACC
TGGTGTCACGGATGAAACCGTATGCCCGCATGGAGGAGTATGAGAGGAACATCGAGGAGATG
GTGGCCCAGCTGAGGAACAGCTCAGAGCTGGCCCAGAGAAAAGTGTGAGGTCAACTTGCAGCT
GTGGATGTCCAACAAGAGGAGCCTGTCTCCCTGGGGCTACAGCATCAACCACGACCCCAGCC
GTATCCCCGTGGACCTGCCGGAGGCACGGTGCCTGTGTCTGGGCTGTTGAACCCCTTCACC
ATGCAGGAGGACCGCAGCATGGTGAGCGTGCCGGTGTTCAGCCAGGTTCCTGTGCGCCGCCG
CCTCTGCCCGCCACCGCCCCGCACAGGGCCTTGCCGCCAGCGCGCAGTCATGGAGACCATCG
CTGTGGGCTGCACCTGCATCTTCTGAATCACCTGGCCCAGAAGCCAGGCCAGCAGCCCGAGA
CCATCCTCCTTGCACCTTTGTGCCAAGAAAAGGCCAAGAAAAGTAAACACTGACTTTTGAAA

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59294

<subunit 1 of 1, 180 aa, 1 stop</pre>

<MW: 20437, pI: 9.58, NX(S/T): 1

MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEEY ERNIEEMVAQLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPSRIPVDLPEARCLCL GCVNPFTMQEDRSMVSVPVFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 75-78

Homologous region to IL-17

amino acids 96-180.

GCGCCGCCAGGCGTAGGCGGGGGGGCCCTTGCGTCTCCCGCTTCCTTGAAAAACCCGGCGGG GCGCCCAAC<u>ATG</u>GCGGGTGGGCGCTGCGGCCCGCAGCTAACGGCGCCTCCTGGCCGCCTGGAT CGCGGCTGTGGCGGCGACGGCAGGCCCCGAGGAGGCCGCGCTGCCGCGGAGCAGAGCCGGG TCCAGCCCATGACCGCCTCCAACTGGACGCTGGTGATGGAGGGCGAGTGGATGCTGAAATTT TACGCCCCATGGTGTCCATCCTGCCAGCAGACTGATTCAGAATGGGAGGCTTTTGCAAAGAA TGGTGAAATACTTCAGATCAGTGTGGGGAAGGTAGATGTCATTCAAGAACCAGGTTTGAGTG GCCGCTTCTTTGTCACCACTCTCCCAGCATTTTTTCATGCAAAGGATGGGATATTCCGCCGT TATCGTGGCCCAGGAATCTTCGAAGACCTGCAGAATTATATCTTAGAGAAGAAATGGCAATC AGTCGAGCCTCTGACTGGCTGGAAATCCCCAGCTTCTCTAACGATGTCTGGAATGGCTGGTC TTTTTAGCATCTCTGGCAAGATATGGCATCTTCACAACTATTTCACAGTGACTCTTGGAATT CCTGCTTGGTGTTCTTATGTGTTTTTCGTCATAGCCACCTTGGTTTTTTGGCCTTTTTATGGG TCTGGTCTTGGTGGTAATATCAGAATGTTTCTATGTGCCACTTCCAAGGCATTTATCTGAGC GTTCTGAGCAGAATCGGAGATCAGAGGAGGCTCATAGAGCTGAACAGTTGCAGGATGCGGAG GAGGAAAAAGATGATTCAAATGAAGAAGAAAACAAAGACAGCCTTGTAGATGATGAAGAAGA GAAAGAAGATCTTGGCGATGAGGATGAAGCAGAGGAAGAAGAGAGGAGGAGGACAACTTGGCTG CTGGTGTGGATGAGGAGAGAGTGAGGCCAATGATCAGGGGCCCCCAGGAGAGGACGGTGTG ACCCGGGAGGAAGTAGAGCCTGAGGAGGCTGAAGAAGGCATCTCTGAGCAACCCTGCCCAGC TGACACAGAGGTGGTGGAAGACTCCTTGAGGCAGCGTAAAAGTCAGCATGCTGACAAGGGAC TG**TAG**ATTTAATGATGCGTTTTCAAGAATACACACCAAAACAATATGTCAGCTTCCCTTTGG CCTGCAGTTTGTACCAAATCCTTAATTTTTCCTGAATGAGCAAGCTTCTCTTAAAAGATGCT CTCTAGTCATTTGGTCTCATGGCAGTAAGCCTCATGTATACTAAGGAGAGTCTTCCAGGTGT GACAATCAGGATATAGAAAAACAAACGTAGTGTTGGGATCTGTTTGGAGACTGGGATGGGAA CAAGTTCATTTACTTAGGGGTCAGAGAGTCTCGACCAGAGGGGGCCATTCCCAGTCCTAATC AGCACCTTCCAGAGACAAGGCTGCAGGCCCTGTGAAATGAAAGCCAAGCAGGAGCCTTGGCT CCTGAGCATCCCCAAAGTGTAACGTAGAAGCCTTGCATCCTTTTCTTGTGTAAAGTATTTAT TTTTGTCAAATTGCAGGAAACATCAGGCACCACAGTGCATGAAAAATCTTTCACAGCTAGAA ATTGAAAGGGCCTTGGGTATAGAGAGCAGCTCAGAAGTCATCCCAGCCCTCTGAATCTCCTG TGCTATGTTTTATTTCTTACCTTTAATTTTTCCAGCATTTCCACCATGGGCATTCAGGCTCT CCACACTCTTCACTATTATCTCTTGGTCAGAGGACTCCAATAACAGCCAGGTTTACATGAAC TGTGTTTGTTCATTCTGACCTAAGGGGTTTAGATAATCAGTAACCATAACCCCTGAAGCTGT GACTGCCAAACATCTCAAATGAAATGTTGTGGCCATCAGAGACTCAAAAGGAAGTAAGGATT **AAGTTTTCTAAGCAATATTTTTCAAGCCAGAAGTCCTCTAAGTCTTGCCAGTACAAGGTAGT** CTTGTGAAGAAAAGTTGAATACTGTTTTGTTTTCATCTCAAGGGGTTCCCTGGGTCTTGAAC TACTTTAATAATAACTAAAAAACCACTTCTGATTTTCCTTCAGTGATGTGCTTTTGGTGAAA GAATTAATGAACTCCAGTACCTGAAAGTGAAAGATTTGATTTTGTTTCCATCTTCTGTAATC TTCCAAAGAATTATATCTTTGTAAATCTCTCAATACTCAATCTACTGTAAGTACCCAGGGAG GCTAATTTCTTT

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56433

<subunit 1 of 1, 349 aa, 1 stop

<MW: 38952, pI: 4.34, NX(S/T): 1

MAGGRCGPQLTALLAAWIAAVAATAGPEEAALPPEQSRVQPMTASNWTLVMEGEWMLKFYAP WCPSCQQTDSEWEAFAKNGEILQISVGKVDVIQEPGLSGRFFVTTLPAFFHAKDGIFRRYRG PGIFEDLQNYILEKKWQSVEPLTGWKSPASLTMSGMAGLFSISGKIWHLHNYFTVTLGIPAW CSYVFFVIATLVFGLFMGLVLVVISECFYVPLPRHLSERSEQNRRSEEAHRAEQLQDAEEEK DDSNEEENKDSLVDDEEEKEDLGDEDEAEEEEEEDNLAAGVDEERSEANDQGPPGEDGVTRE EVEPEEAEEGISEQPCPADTEVVEDSLRQRKSQHADKGL

Important features:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 191-211

N-glycosylation site.

amino acids 46-49

Thioredoxin family proteins. (homologous region to disulfide isomerase) amino acids 56-72

Flavodoxin proteins

amino acids 173-187

ATCTGGTTGAACTACTTAAGCTTAATTTGTTAAACTCCGGTAAGTACCTAGCCCACATGATT CAAATGCTATATCTATTCAGGGGCTCTCAAGAACA<u>ATG</u>GAATATCATCCTGATTTAGAAAAT TTGGATGAAGATGGATATACTCAATTACACTTCGACTCTCAAAGCAATACCAGGATAGCTGT TGTTTCAGAGAAAGGATCGTGTGCTGCATCTCCTTCGTGGCGCCTCATTGCTGAATTTTGG GAATCCTATGCTTGGTAATACTGGTGATAGCTGTGGTCCTGGGTACCATGGGGGTTCTTTCC AGCCCTTGTCCTCAATTGGATTATATATGAGAAGAGCTGTTATCTATTCAGCATGTCACT AAATTCCTGGGATGGAAGTAAAAGACAATGCTGGCAACTGGGCTCTAATCTCCTAAAGATAG ACAGCTCAAATGAATTGGGATTTATAGTAAAACAAGTGTCTTCCCAACCTGATAATTCATTT CTCTTCTAACTTATTTCAGATCAGAACCACAGCTACCCAAGAAAACCCATCTCCAAATTGTG TATGGATTCACGTGTCAGTCATTTATGACCAACTGTGTAGTGTGCCCTCATATAGTATTTGT AGGAGGACAGAAACAGAACAGAAAAGAGTAACAGCTGAGGTCAAGATAAATGCAGAAAATG TTTAGAGAGCTTGGCCAACTGTAATCTTAACCAAGAAATTGAAGGGAGAGGCTGTGATTTCT CACTTTGTTACCCAGGCTGGAGTGCAGTGGCACAATCTCGACTCACTGCAGCTATCTCTCGC CTCAGCCCCTCAAGTAGCTGGGACTACAGGTGCATGCCACCATGCCAGGCTAATTTTTGGTG TTTTTTGTAGAGACTGGGTTTTGCCATGTTGACCAAGCTGGTCTCTAACTCCTGGGCTTAAG TGATCTGCCCGCCTTGGCCTCCCAAAGTGCTGGGATTACAGATGTGAGCCACCACACCTGGC CCCAAGCTTGAATTTTCATTCTGCCATTGACTTGGCATTTACCTTGGGTAAGCCATAAGCGA ATCTTAATTTCTGGCTCTATCAGAGTTGTTTCATGCTCAACAATGCCATTGAAGTGCACGGT GTGTTGCCACGATTTGACCCTCAACTTCTAGCAGTATATCAGTTATGAACTGAGGGTGAAAT ATATTTCTGAATAGCTAAATGAAGAAATGGGAAAAAATCTTCACCACAGTCAGAGCAATTTT ATTATTTTCATCAGTATGATCATATTATGATTATCATCTTAGTAAAAAGCAGGAACTCCTA CTTTTTCTTTATCAATTAAATAGCTCAGAGAGTACATCTGCCATATCTCTAATAGAATCTTT TTTTTTTTTTTTTTTTGAGACAGAGTTTCGCTCTTGTTGCCCAGGCTGGAGTGCAACGG CACGATCTCGGCTCACCGCAACCTCCGCCCCCTGGGTTCAAGCAATTCTCCTGCCTCAGCCT CCCAAGTAGCTGGGATTACAGTCAGGCACCACCACCCGGCTAATTTTGTATTTTTAGT AGAGACAGGGTTTCTCCATGTCGGTCAGGGTAGTCCCGAACTCCTGACCTCAAGTGATCTGC CTGCCTCGGCCTCCCAAGTGCTGGGATTACAGGCGTGAGCCACCTGCACCCAGCCTAGAATCT TGTATAATATGTAATTGTAGGGAAACTGCTCTCATAGGAAAGTTTTCTGCTTTTTAAATACA ACAAGTATTAACATTTTGGAATATGTTTTATTAGTTTTGTGATGTACTGTTTTACAATTTTT ACCATTTTTTTCAGTAATTACTGTAAAATGGTATTATTGGAATGAAACTATATTTCCTCATG TGCTGATTTGTCTTATTTTTTTCATACTTTCCCACTGGTGCTATTTTTATTTCCAATGGATA TTTCTGTATTACTAGGGAGGCATTTACAGTCCTCTAATGTTGATTAATATGTGAAAAAGAAAT TGTACCAATTTTACTAAATTATGCAGTTTAAAATGGATGATTTTATGTTATGTGGATTTCAT

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA53912</pre>

<subunit 1 of 1, 201 aa, 1 stop

<MW: 22563, pI: 4.87, NX(S/T): 1

MEYHPDLENLDEDGYTQLHFDSQSNTRIAVVSEKGSCAASPPWRLIAVILGILCLVILVIAV VLGTMGVLSSPCPPNWIIYEKSCYLFSMSLNSWDGSKRQCWQLGSNLLKIDSSNELGFIVKQ VSSQPDNSFWIGLSRPQTEVPWLWEDGSTFSSNLFQIRTTATQENPSPNCVWIHVSVIYDQL CSVPSYSICEKKFSM

Important features:

Type II transmembrane domain:

amino acids 45-65

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 197-200

N-myristoylation sites.

amino acids 35-40 and 151-156

Homologous region to LDL receptor

amino acids 34-67 and 70-200.

FIGURE 203A

GGAAGGGGAGGAGCAGGCCACACAGGCCAGGCCGGTGAGGGACCTGCCCAGACCTGGAGGG TCTCGCTCTGTCACACAGGCTGGAGTGCAGTGGTGTGATCTTGGCTCATCGTAACCTCCACC TCCCGGGTTCAAGTGATTCTCATGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGTGGTGAC ${\tt TTCCAAGAGTGACTCCGTCGGAGGAAA} \underline{{\tt ATC}} {\tt ACTCCCCAGTCGCTGCTGCAGACGACACTGTT}$ CCTGCTGAGTCTGCTCCTGGTCCAAGGTGCCCACGGCAGGGGCCACAGGGAAGACTTTC GCTTCTGCAGCCAGCGGAACCAGACACAGGAGCAGCCTCCACTACAAACCCACACCAGAC CTGCGCATCTCCATCGAGAACTCCGAAGAGGCCCTCACAGTCCATGCCCCTTTCCCTGCAGC CCACCCTGCTTCCCGATCCTTCCCTGACCCCAGGGGCCTCTACCACTTCTGCCTCTACTGGA ACCGACATGCTGGGAGATTACATCTTCTCTATGGCAAGCGTGACTTCTTGCTGAGTGACAAA GCCTCTAGCCTCTGCTTCCAGCACCAGGAGGAGGAGCCTGGCTCAGGGCCCCCCGCTGTT AGCCACTTCTGTCACCTCCTGGTGGAGCCCTCAGAACATCAGCCTGCCCAGTGCCGCCAGCT TCACCTTCTCCTTCCACAGTCCTCCCCACACGGCCGCTCACAATGCCTCGGTGGACATGTGC GAGCTCAAAAGGGACCTCCAGCTGCTCAGCCAGTTCCTGAAGCATCCCCAGAAGGCCTCAAG GAGGCCCTCGGCTGCCCCCCCCAGCCAGCAGTTGCAGAGCCTGGAGTCGAAACTGACCTCTG TGAGATTCATGGGGGACATGGTGTCCTTCGAGGAGGACCGGATCAACGCCACGGTGTGGAAG CTCCAGCCCACAGCCGGCCTCCAGGACCTGCACATCCACTCCCGGCAGGAGGAGGAGCAGAG CGAGATCATGGAGTACTCGGTGCTGCCTCGAACACTCTTCCAGAGGACGAAAGGCCGGA GCGGGGAGGCTGAGAAGAGACTCCTCCTGGTGGACTTCAGCAGCCCAAGCCCTGTTCCAGGAC AAGAATTCCAGCCAAGTCCTGGGTGAGAAGGTCTTGGGGATTGTGGTACAGAACACCAAAGT AGCCAACCTCACGGAGCCCGTGGTGCTCACTTTCCAGCACCAGCTACAGCCGAAGAATGTGA CTCTGCAATGTGTGTTCTGGGTTGAAGACCCCACATTGAGCAGCCCGGGGCATTGGAGCAGT GCTGGGTGTGAGACCGTCAGGAGAGAACCCAAACATCCTGCTTCTGCAACCACTTGACCTA CTTTGCAGTGCTGATGGTCTCCTCGGTGGAGGTGGACGCCGTGCACAAGCACTACCTGAGCC CTCTGCTCCAGGGTGCCCTGCCGTGCAGGAGGAAACCTCGGGACTACACCATCAAGGTGCA CATGAACCTGCTGGCCGTCTTCCTGCTGGACACGAGCTTCCTGCTCAGCGAGCCGGTGG CCCTGACAGGCTCTGAGGCTGCCGAGCCAGTGCCATCTTCCTGCACTTCTCCCTGCTC ACCTGCCTTTCCTGGATGGGCCTCGAGGGGTACAACCTCTACCGACTCGTGGTGGAGGTCTT TGGCACCTATGTCCCTGGCTACCTACTCAAGCTGAGCGCCATGGGCTGGGGCTTCCCCATCT TTCTGGTGACGCTGGTGGCCCTGGTGGATGTGGACAACTATGGCCCCATCATCTTGGCTGTG CATAGGACTCCAGAGGGCGTCATCTACCCTTCCATGTGCTGGATCCGGGACTCCCTGGTCAG CTACATCACCAACCTGGGCCTCTTCAGCCTGGTGTTTCTGTTCAACATGGCCATGCTAGCCA CCATGGTGGTGCAGATCCTGCGGCTGCGCCCCCACACCCCAAAAGTGGTCACATGTGCTGACA CTGCTGGGCCTCAGCCTGGTCCTTGGCCTGCCCTGGGCCTTGATCTTCTTCTCCTTTGCTTC TGGCACCTTCCAGCTTGTCGTCCTCTACCTTTTCAGCATCATCACCTCCTTCCAAGGCTTCC TCATCTTCATCTGGTACTGGTCCATGCGGCTGCAGGCCCGGGGTGGCCCCTCCCCTCTGAAG $\mathtt{AGCAACTCAGACAGCGCCAGGCTCCCCATCAGCTCGGGCAGCACCTCGTCCAGCCGCATC}$ **G**GCCTCCAGCCCACCTGCCCATGTGATGAAGCAGAGATGCGGCCTCGTCGCACACTGCCTGT GGCCCCCGAGCCAGGCCCAGGCCAGGCCAGTCAGCCGCAGACTTTGGAAAGCCCAACGACC ATGGAGAGATGGGCCGTTGCCATGGTGGACGGACTCCCGGGCTGGGCTTTTGAATTGGCCTT GGGGACTACTCGGCTCTCACTCAGCTCCCACGGGACTCAGAAGTGCGCCGCCATGCTGCCTA GGGTACTGTCCCACATCTGTCCCAACCCAGCTGGAGGCCTGGTCTCTCCTTACAACCCCTG GGCCCAGCCCTCATTGCTGGGGGCCCAGGCCTTGGATCTTGAGGGTCTGGCACATCCTTAATC CTGTGCCCTGCCTGGGACAGAATGTGGCTCCAGTTGCTCTGTCTCTCGTGGTCACCCTGA GGGCACTCTGCATCTGTCATTTTAACCTCAGGTGGCACCCAGGGCGAATGGGGCCCAGG GCAGACCTTCAGGGCCAGAGCCCTGGCGGAGGAGGAGCCCTTTGCCAGGAGCACAGCAGCAG CCCTGGGGTTCTCCTCTCCCAGGGCCTCCTTGCTCCTTCGTTCACAGCTGGGGGTCCCC GATTCCAATGCTGTTTTTTGGGGAGTGGTTTCCAGGAGCTGCCTGGTGTCTGCTGTAAATGT TTGTCTACTGCACAAGCCTCGGCCTGCCCCTGAGCCAGGCTCGGTACCGATGCGTGGGCTGG GCTAGGTCCCTCTGTCCATCTGGGCCTTTGTATGAGCTGCATTGCCCTTGCTCACCCTGACC AAGCACACGCCTCAGAGGGGCCCTCAGCCTCTCCTGAAGCCCTCTTGTGGCAAGAACTGTGG ACCATGCCAGTCCGTCTGGTTTCCATCCCACCACTCCAAGGACTGAGACTGACCTCCTCTG GTGACACTGGCCTAGAGCCTGACACTCTCCTAAGAGGTTCTCTCCAAGCCCCCAAATAGCTC



PCT/US99/05028

FIGURE 203B

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50921</pre>

<subunit 1 of 1, 693 aa, 1 stop

<MW: 77738, pI: 8.87, NX(S/T): 7

MTPQSLLQTTLFLLSLLFLVQGAHGRGHREDFRFCSQRNQTHRSSLHYKPTPDLRISIENSE EALTVHAPFPAAHPASRSFPDPRGLYHFCLYWNRHAGRLHLLYGKRDFLLSDKASSLLCFQH QEESLAQGPPLLATSVTSWWSPQNISLPSAASFTFSFHSPPHTAAHNASVDMCELKRDLQLL SQFLKHPQKASRRPSAAPASQQLQSLESKLTSVRFMGDMVSFEEDRINATVWKLQPTAGLQD LHIHSRQEEEQSEIMEYSVLLPRTLFQRTKGRSGEAEKRLLLVDFSSQALFQDKNSSQVLGE KVLGIVVQNTKVANLTEPVVLTFQHQLQPKNVTLQCVFWVEDPTLSSPGHWSSAGCETVRRE TQTSCFCNHLTYFAVLMVSSVEVDAVHKHYLSLLSYVGCVVSALACLVTIAAYLCSRVPLPC RRKPRDYTIKVHMNLLLAVFLLDTSFLLSEPVALTGSEAGCRASAIFLHFSLLTCLSWMGLE GYNLYRLVVEVFGTYVPGYLLKLSAMGWGFPIFLVTLVALVDVDNYGPIILAVHRTPEGVIY PSMCWIRDSLVSYITNLGLFSLVFLFNMAMLATMVVQILRLRPHTQKWSHVLTLLGLSLVLG LPWALIFFSFASGTFQLVVLYLFSIITSFQGFLIFIWYWSMRLQARGGPSPLKSNSDSARLP ISSGSTSSSRI

Important features:

Signal peptide:

amino acids 1-25

Putative transmembrane domains:

amino acids 382-398, 402-420, 445-468, 473-491, 519-537, 568-590 and 634-657

Microbodies C-terminal targeting signal.

amino acids 691-693

cAMP- and cGMP-dependent protein kinase phosphorylation sites. amino acids 198-201 and 370-373

N-glycosylation sites.

amino acids 39-42, 148-151, 171-174, 234-237, 303-306, 324-327 and 341-344

G-protein coupled receptors family 2 proteins

amino acids 475-504

WO 99/46281 PCT/US99/05028

FIGURE 205

TGCCTGGCCTGCCTTGTCAACAATGCCGCTTACTCTGCTTCCAGGTTGCCCTGCCTTGCAGA
GGAAANCNTCGGGACTACACCNTCAAGTGCACATGAACCTGCTGCTGGCCGTCTTCCTGCTG
GACACGAGCTTCCTGCTCAGCGNAGCCGGTGGCCCTGACAGGCTCTGAAGGCTGGCCGA
GCCAGTGCCATCTTCCTGCACTTCTCCTGCTCACCTGCCTTTCCTGGATGGGCCTCGAGGGG
TACAACCTCTACCGACTCGTGGTGGAGGTCTTTGGCACCTATGTCCCTGGCTACCTAAC
GCTGAGCGCCATGGGGGGCTTCCCCATCTTTCTGGTGACGCTGGTGGCCCTGGTGGATG
TGGACAACTATGGCCCCATCATCTTGGCTGTGCATAGGACTCCAGAGGGCGTCATCTACCCT
TCCATGTGCTGGATCCGGGACTCCCTGGTCAGCTACATCACCAACCTGGGCCTCTTCAGCCT
GGTGTTTCTGTTCAACATGG



CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCTGGTTCAGGTCCA GGTTTTGCTTTGATCCTTTTCAAAAACTGGAGACACAGAAGAGGGCTCTAGGAAAAAGTTTT GGATGGGATTATGTGGAAACTACCCTGCGATTCTCTGCTGCCAGAGCAGGCTCGGCGCTTCC ACCCCAGTGCAGCCTTCCCCTGGCGGTGGTGAAAGAGACTCGGGAGTCGCTGCTTCCAAAGT GCCCGCCGTGAGTGAGCTCTCACCCCAGTCAGCCAAATGAGCCTCTTCGGGCTTCTCCTGCT GACATCTGCCCTGGCCGGCCAGAGACAGGGGGACTCAGGCGGAATCCAACCTGAGTAGAAT TCCAGTTTTCCAGCAACAAGGAACAGAACGGAGTACAAGATCCTCAGCATGAGAGAATTATT ACTGTGTCTACTAATGGAAGTATTCACAGCCCAAGGTTTCCTCATACTTATCCAAGAAATAC GGTCTTGGTATGGAGATTAGTAGCAGTAGAGGAAAATGTATGGATACAACTTACGTTTGATG AAAGATTTGGGCTTGAAGACCCAGAAGATGACATATGCAAGTATGATTTTGTAGAAGTTGAG GAACCCAGTGATGGAACTATATTAGGGCGCTGGTGTGTTCTGGTACTGTACCAGGAAAACA GATTTCTAAAGGAAATCAAATTAGGATAAGATTTGTATCTGATGAATATTTTCCTTCTGAAC CAGGGTTCTGCATCCACTACAACATTGTCATGCCACAATTCACAGAAGCTGTGAGTCCTTCA GTGCTACCCCCTTCAGCTTTGCCACTGGACCTGCTTAATAATGCTATAACTGCCTTTAGTAC CTTGGAAGACCTTATTCGATATCTTGAACCAGAGAGATGGCAGTTGGACTTAGAAGATCTAT ATAGGCCAACTTGGCAACTTCTTGGCAAGGCTTTTGTTTTTGGAAGAAAATCCAGAGTGGTG GATCTGAACCTTCTAACAGAGGAGGTAAGATTATACAGCTGCACACCTCGTAACTTCTCAGT GTCCATAAGGGAAGAACTAAAGAGAACCGATACCATTTTCTGGCCAGGTTGTCTCCTGGTTA AGCAAAGTTACTAAAAAATACCACGAGGTCCTTCAGTTGAGACCAAAGACCGGTGTCAGGGG GAGGGAGCACAGGAGGATAGCCGCATCACCACCAGCAGCTCTTGCCCAGAGCTGTGCAGTGC AGTGGCTGATTCTATTAGAGAACGTATGCGTTATCTCCATCCTTAATCTCAGTTGTTTGCTT CAAGGACCTTTCATCTTCAGGATTTACAGTGCATTCTGAAAGAGGAGACATCAAACAGAATT AGGAGTTGTGCAACAGCTCTTTTGAGAGGAGGCCTAAAGGACAGGAGAAAAGGTCTTCAATC GTGGAAAGAAATTAAATGTTGTATTAAATAGATCACCAGCTAGTTTCAGAGTTACCATGTA CGTATTCCACTAGCTGGGTTCTGTATTTCAGTTCTTTCGATACGGCTTAGGGTAATGTCAGT ACAGGAAAAAACTGTGCAAGTGAGCACCTGATTCCGTTGCCTTGACTCTAAAGCTCC ATATGTAAACCAGAACATTCTATGTACTACAAACCTGGTTTTTAAAAAGGAACTATGTTGCT ATGAATTAAACTTGTGTCATGCTGATAGGACAGACTGGATTTTTCATATTTCTTATTAAAAT TTCTGCCATTTAGAAGAAGAGAACTACATTCATGGTTTGGAAGAGATAAACCTGAAAAGAAG AGTGGCCTTATCTTCACTTTATCGATAAGTCAGTTTATTTGTTTCATTGTGTACATTTTTAT ATTCTCCTTTTGACATTATAACTGTTGGCTTTTCTAATCTTGTTAAATATATCTATTTTTAC CAAAGGTATTTAATATTCTTTTTTATGACAACTTAGATCAACTATTTTTAGCTTGGTAAATT TTTCTAAACACAATTGTTATAGCCAGAGGAACAAAGATGATATAAAATATTGTTGCTCTGAC **AAAAATACATGTATTTCATTCTCGTATGGTGCTAGAGTTAGATTAATCTGCATTTTAAAAAA** CTGAATTGGAATAGAATTGGTAAGTTGCAAAGACTTTTTGAAAATAATTAAATTATCATATC TTCCATTCCTGTTATTGGAGATGAAAATAAAAAGCAACTTATGAAAGTAGACATTCAGATCC AGCCATTACTAACCTATTCCTTTTTTGGGGAAATCTGAGCCTAGCTCAGAAAAACATAAAGC ACCTTGAAAAAGACTTGGCAGCTTCCTGATAAAGCGTGCTGTGCTGTGCAGTAGGAACACAT CCTATTTATTGTGATGTTGTGGTTTTATTATCTTAAACTCTGTTCCATACACTTGTATAAAT ACATGGATATTTTTATGTACAGAAGTATGTCTCTTAACCAGTTCACTTATTGTACTCTGGCA ATTTAAAAGAAAATCAGTAAAATATTTTGCTTGTAAAATGCTTAATATNGTGCCTAGGTTAT GTGGTGACTATTTGAATCAAAAATGTATTGAATCATCAAATAAAAGAATGTGGCTATTTTGG GGAGAAAATTAAAAAAAAAAAAAAAAAAAAGGTTTAGGGATAACAGGGTAATGCGGCC

MSLFGLLLLTSALAGQRQGTQAESNLSSKFQFSSNKEQNGVQDPQHERIITVSTNGSIHSPR FPHTYPRNTVLVWRLVAVEENVWIQLTFDERFGLEDPEDDICKYDFVEVEEPSDGTILGRWC GSGTVPGKQISKGNQIRIRFVSDEYFPSEPGFCIHYNIVMPQFTEAVSPSVLPPSALPLDLL NNAITAFSTLEDLIRYLEPERWQLDLEDLYRPTWQLLGKAFVFGRKSRVVDLNLLTEEVRLY SCTPRNFSVSIREELKRTDTIFWPGCLLVKRCGGNCACCLHNCNECQCVPSKVTKKYHEVLQ LRPKTGVRGLHKSLTDVALEHHEECDCVCRGSTGG



CCCATCTCAAGCTGATCTTGGCACCTCTCATGCTCTGCTCTTCAACCAGACCTCTACATT CCATTTTGGAAGAGACTAAAAAATCGTGTTTCCAATGTGGACACTGAAGAGACAAATTCTTA TCCTTTTTAACATAATCCTAATTTCCAAACTCCTTGGGGCTAGATGGTTTCCTAAAACTCTG CCCTGTGATGTCACTCTGGATGTTCCAAAGAACCATGTGATCGTGGACTGCACAGACAAGCA TTTGACAGAAATTCCTGGAGGTATTCCCACGAACACCACGAACCTCACCCTCACCATTAACC ACATACCAGACATCTCCCCAGCGTCCTTTCACAGACTGGACCATCTGGTAGAGATCGATTTC AGATGCAACTGTGTACCTATTCCACTGGGGTCAAAAAACAACATGTGCATCAAGAGGCTGCA AGCTACTAGAGATACCGCAGGGCCTCCCGCCTAGCTTACAGCTTCTCAGCCTTGAGGCCAAC AACATCTTTTCCATCAGAAAAGAGAATCTAACAGAACTGGCCAACATAGAAATACTCTACCT GGGCCAAAACTGTTATTATCGAAATCCTTGTTATGTTTCATATTCAATAGAGAAAGATGCCT TCCTAAACTTGACAAAGTTAAAAGTGCTCTCCCTGAAAGATAACAATGTCACAGCCGTCCCT ACTGTTTTGCCATCTACTTTAACAGAACTATATCTCTACAACAACATGATTGCAAAAATCCA AGAAGATGATTTTAATAACCTCAACCAATTACAAATTCTTGACCTAAGTGGAAATTGCCCTC GTTGTTATAATGCCCCATTTCCTTGTGCGCCGTGTAAAAATAATTCTCCCCTACAGATCCCT GTAAATGCTTTTGATGCGCTGACAGAATTAAAAGTTTTACGTCTACACAGTAACTCTCTTCA GCATGTGCCCCCAAGATGGTTTAAGAACATCAACAAACTCCAGGAACTGGATCTGTCCCAAA ACTTCTTGGCCAAAGAAATTGGGGATGCTAAATTTCTGCATTTTCTCCCCAGCCTCATCCAA TTGGATCTGTCTTTCAATTTTGAACTTCAGGTCTATCGTGCATCTATGAATCTATCACAAGC ATTTTCTTCACTGAAAAGCCTGAAAATTCTGCGGATCAGAGGATATGTCTTTAAAGAGTTGA AAAGCTTTAACCTCTCGCCATTACATAATCTTCAAAATCTTGAAGTTCTTGATCTTGGCACT AACTTTATAAAAATTGCTAACCTCAGCATGTTTAAACAATTTAAAAGACTGAAAGTCATAGA TCTTTCAGTGAATAAAATATCACCTTCAGGAGATTCAAGTGAAGTTGGCTTCTGCTCAAATG CCAGAACTTCTGTAGAAAGTTATGAACCCCAGGTCCTGGAACAATTACATTATTTCAGATAT GATAAGTATGCAAGGAGTTGCAGATTCAAAAACAAAGAGGCTTCTTTCATGTCTGTTAATGA AAGCTGCTACAAGTATGGGCAGACCTTGGATCTAAGTAAAAATAGTATATTTTTTTGTCAAGT CCTCTGATTTTCAGCATCTTTCCTTCAAATGCCTGAATCTGTCAGGAAATCTCATTAGC CAAACTCTTAATGGCAGTGAATTCCAACCTTTAGCAGAGCTGAGATATTTGGACTTCTCCAA CAACCGGCTTGATTTACTCCATTCAACAGCATTTGAAGAGCTTCACAAACTGGAAGTTCTGG ATATAAGCAGTAATAGCCATTATTTTCAATCAGAAGGAATTACTCATATGCTAAACTTTACC AAGAACCTAAAGGTTCTGCAGAAACTGATGATGAACGACAATGACATCTCTTCCTCCACCAG CAGGACCATGGAGAGTGAGTCTCTTAGAACTCTGGAATTCAGAGGAAATCACTTAGATGTTT TATGGAGAGAGGTGATAACAGATACTTACAATTATTCAAGAATCTGCTAAAATTAGAGGAA TTAGACATCTCTAAAAATTCCCTAAGTTTCTTGCCTTCTGGAGTTTTTGATGGTATGCCTCC AAATCTAAAGAATCTCTCTTTGGCCAAAAATGGGCTCAAATCTTTCAGTTGGAAGAAACTCC AGATTATCCAACTGTTCCAGAAGCCTCAAGAATCTGATTCTTAAGAATAATCAAATCAGGAG TCTGACGAAGTATTTTCTACAAGATGCCTTCCAGTTGCGATATCTGGATCTCAGCTCAAATA **AAA**TCCAGATGATCCAAAAGACCAGCTTCCCAGAAAATGTCCTCAACAATCTGAAGATGTTG CCATACGGAGGTGACTATTCCTTACCTGGCCACAGATGTGACTTGTGTGGGGCCAGGAGCAC ACAAGGGCCAAAGTGTGATCTCCCTGGATCTGTACACCTGTGAGTTAGATCTGACTAACCTG ATTCTGTTCTCACTTTCCATATCTGTATCTCTCTTTCTCATGGTGATGATGACAGCAAGTCA CCTCTATTTCTGGGATGTGTGGTATATTTACCATTTCTGTAAGGCCAAGATAAAGGGGTATC AGCGTCTAATATCACCAGACTGTTGCTATGATGCTTTTATTGTGTATGACACTAAAGACCCA GCTGTGACCGAGTGGGTTTTGGCTGAGCTGGTGGCCAAACTGGAAGACCCAAGAGAGAAACA TTTTAATTTATGTCTCGAGGAAAGGGACTGGTTACCAGGGCAGCCAGTTCTGGAAAACCTTT GAAAATTTTAAGATAGCATTTTACTTGTCCCATCAGAGGCTCATGGATGAAAAAGTTGATGT GATTATCTTGATATTTCTTGAGAAGCCCTTTCAGAAGTCCAAGTTCCTCCAGCTCCGGAAAA GGCTCTGTGGGAGTTCTGTCCTTGAGTGGCCAACAAACCCGCAAGCTCACCCATACTTCTGG CAGTGTCTAAAGAACGCCCTGGCCACAGACAATCATGTGGCCTATAGTCAGGTGTTCAAGGA AACGGTCTAGCCCTTCTTTGCAAAACACAACTGCCTAGTTTACCAAGGAGAGGCCTGGC



MVFPMWTLKRQILILFNIILISKLLGARWFPKTLPCDVTLDVPKNHVIVDCTDKHLTEIPGG IPTNTTNLTLTINHIPDISPASFHRLDHLVEIDFRCNCVPIPLGSKNNMCIKRLQIKPRSFS GLTYLKSLYLDGNQLLEIPQGLPPSLQLLSLEANNIFSIRKENLTELANIEILYLGQNCYYR NPCYVSYSIEKDAFLNLTKLKVLSLKDNNVTAVPTVLPSTLTELYLYNNMIAKIQEDDFNNL NOLQILDLSGNCPRCYNAPFPCAPCKNNSPLQIPVNAFDALTELKVLRLHSNSLQHVPPRWF KNINKLOELDLSQNFLAKEIGDAKFLHFLPSLIQLDLSFNFELQVYRASMNLSQAFSSLKSL KILRIRGYVFKELKSFNLSPLHNLQNLEVLDLGTNFIKIANLSMFKQFKRLKVIDLSVNKIS PSGDSSEVGFCSNARTSVESYEPQVLEQLHYFRYDKYARSCRFKNKEASFMSVNESCYKYGQ TLDLSKNSIFFVKSSDFQHLSFLKCLNLSGNLISQTLNGSEFQPLAELRYLDFSNNRLDLLH STAFEELHKLEVLDISSNSHYFQSEGITHMLNFTKNLKVLQKLMMNDNDISSSTSRTMESES LRTLEFRGNHLDVLWREGDNRYLQLFKNLLKLEELDISKNSLSFLPSGVFDGMPPNLKNLSL AKNGLKSFSWKKLQCLKNLETLDLSHNQLTTVPERLSNCSRSLKNLILKNNQIRSLTKYFLQ DAFQLRYLDLSSNKIQMIQKTSFPENVLNNLKMLLLHHNRFLCTCDAVWFVWWVNHTEVTIP YLATDVTCVGPGAHKGQSVISLDLYTCELDLTNLILFSLSISVSLFLMVMMTASHLYFWDVW YIYHFCKAKIKGYQRLISPDCCYDAFIVYDTKDPAVTEWVLAELVAKLEDPREKHFNLCLEE RDWLPGQPVLENLSQSIQLSKKTVFVMTDKYAKTENFKIAFYLSHQRLMDEKVDVIILIFLE KPFQKSKFLQLRKRLCGSSVLEWPTNPQAHPYFWQCLKNALATDNHVAYSQVFKETV

FIGURE 210A

GGGTACCATTCTGCGCTGCTGCAAGTTACGGAATGAAAATTAGAACAACAGAAACAACAGAAAC AACATGTTCCTTCAGTCGTCAATGCTGACCTGCATTTTCCTGCTAATATCTGGTTCCTGTGA GTTATGCGCCGAAGAAATTTTTCTAGAAGCTATCCTTGTGATGAGAAAAAGCAAAATGACT CAGTTATTGCAGAGTGCAGCAATCGTCGACTACAGGAAGTTCCCCAAACGGTGGGCAAATAT GCTGCAAAATCTCACTAAAATAAATCTAAACCACAACCCCAATGTACAGCACCAGAACGGAA ATCCCGGTATACAATCAAATGGCTTGAATATCACAGACGGGGCATTCCTCAACCTAAAAAAC CTAAGGGAGTTACTGCTTGAAGACAACCAGTTACCCCAAATACCCTCTGGTTTGCCAGAGTC TTTGACAGAACTTAGTCTAATTCAAAACAATATATACAACATAACTAAAGAGGGCATTTCAA GACTTATAAACTTGAAAAATCTCTATTTGGCCTGGAACTGCTATTTTAACAAAGTTTGCGAG AAAACTAACATAGAAGATGGAGTATTTGAAACGCTGACAAATTTGGAGTTGCTATCACTATC TTTCAATTCTCTTTCACACGTGCCACCCAAACTGCCAAGCTCCCTACGCAAACTTTTTCTGA GCAACACCCAGATCAAATACATTAGTGAAGAAGATTTCAAGGGATTGATAAATTTAACATTA CTAGATTTAAGCGGGAACTGTCCGAGGTGCTTCAATGCCCCATTTCCATGCGTGCCTTGTGA TGGTGGTGCTTCAATTAATATAGATCGTTTTGCTTTTCAAAACTTGACCCAACTTCGATACC TAAACCTCTCTAGCACTTCCCTCAGGAAGATTAATGCTGCCTGGTTTAAAAATATGCCTCAT CTGAAGGTGCTGGATCTTGAATTCAACTATTTAGTGGGAGAAATAGTCTCTGGGGCATTTTT AACGATGCTGCCCCGCTTAGAAATACTTGACTTGTCTTTTAACTATATAAAGGGGAGTTATC CACAGCATATTAATATTTCCAGAAACTTCTCTAAACTTTTGTCTCTACGGGCATTGCATTTA AGAGGTTATGTGTTCCAGGAACTCAGAGAAGATGATTTCCAGCCCCTGATGCAGCTTCCAAA CTTATCGACTATCAACTTGGGTATTAATTTTATTAAGCAAATCGATTTCAAACTTTTCCAAA ATTTCTCCAATCTGGAAATTATTTACTTGTCAGAAAACAGAATATCACCGTTGGTAAAAGAT ACCCGGCAGAGTTATGCAAATAGTTCCTCTTTTCAACGTCATATCCGGAAACGACGCTCAAC AGATTTTGAGTTTGACCCACATTCGAACTTTTATCATTTCACCCGTCCTTTAATAAAGCCAC AATGTGCTGCTTATGGAAAAGCCTTAGATTTAAGCCTCAACAGTATTTTCTTCATTGGGCCA AGTGTTAAGTGGAACTGAATTTTCAGCCATTCCTCATGTCAAATATTTTGGATTTGACAAACA ATAGACTAGACTTTGATAATGCTAGTGCTCTTACTGAATTGTCCGACTTGGAAGTTCTAGAT CTCAGCTATAATTCACACTATTTCAGAATAGCAGGCGTAACACATCATCTAGAATTTATTCA AAATTTCACAAATCTAAAAGTTTTAAACTTGAGCCACAACAACATTTATACTTTAACAGATA AGTATAACCTGGAAAGCAAGTCCCTGGTAGAATTAGTTTTCAGTGGCAATCGCCTTGACATT TTGTGGAATGATGACAACAGGTATATCTCCATTTTCAAAGGTCTCAAGAATCTGACACG TCTGGATTTATCCCTTAATAGGCTGAAGCACATCCCAAATGAAGCATTCCTTAATTTGCCAG CGAGTCTCACTGAACTACATATAAATGATAATGTTAAAGTTTTTTAACTGGACATTACTC TAGCCTATCTGACTTTACATCTTCCCTTCGGACACTGCTGAGTCATAACAGGATTTCCC ACCTACCCTCTGGCTTTCTTCTGAAGTCAGTAGTCTGAAGCACCTCGATTTAAGTTCCAAT CTGCTAAAAACAATCAACAAATCCGCACTTGAAACTAAGACCACCACCAAATTATCTATGTT ATGAACATCTGAATGTCAAAATTCCCAGACTGGTAGATGTCATTTGTGCCAGTCCTGGGGAT CAAAGAGGGAAGAGTATTGTGAGTCTGGAGCTAACAACTTGTGTTTCAGATGTCACTGCAGT GATATTATTTTTCTTCACGTTCTTTATCACCACCATGGTTATGTTGGCTGCCCTGGCTCACC ATTTGTTTTACTGGGATGTTTGGTTTATATATATGTGTGTTTAGCTAAGGTAAAAGGCTAC AGGTCTCTTTCCACATCCCAAACTTTCTATGATGCTTACATTTCTTATGACACCAAAGATGC CTCTGTTACTGACTGGGTGATAAATGAGCTGCGCTACCACCTTGAAGAGAGCCGAGACAAAA ACGTTCTCCTTTGTCTAGAGGAGGGGATTGGGACCCGGGATTGGCCATCATCGACAACCTC ATGCAGAGCATCAACCAAAGCAAGAAAACAGTATTTGTTTTAACCAAAAAATATGCAAAAAG CTGGAACTTTAAAACAGCTTTTTACTTGGCTTTGCAGAGGCTAATGGATGAGAACATGGATG TGATTATATTTATCCTGCTGGAGCCAGTGTTACAGCATTCTCAGTATTTGAGGCTACGGCAG CGGATCTGTAAGAGCTCCATCCTCCAGTGGCCTGACAACCCGAAGGCAGAAGGCTTGTTTTG ATTCCATTAAGCAATAC<u>TAA</u>CTGACGTTAAGTCATGATTTCGCGCCATAATAAAGATGCAAA GGAATGACATTTCTGTATTAGTTATCTATTGCTATGTAACAAATTATCCCAAAACTTAGTGG TTTAAAACAACACATTTGCTGGCCCACAGTTTTTGAGGGTCAGGAGTCCAGGCCCAGCATAA



FIGURE 210B





MENMFLQSSMLTCIFLLISGSCELCAEENFSRSYPCDEKKQNDSVIAECSNRRLQEVPQTVG ${\tt KYVTELDLSDNFITHITNESFQGLQNLTKINLNHNPNVQHQNGNPGIQSNGLNITDGAFLNL}$ KNLRELLLEDNQLPQIPSGLPESLTELSLIQNNIYNITKEGISRLINLKNLYLAWNCYFNKV CEKTNIEDGVFETLTNLELLSLSFNSLSHVPPKLPSSLRKLFLSNTQIKYISEEDFKGLINL TLLDLSGNCPRCFNAPFPCVPCDGGASINIDRFAFQNLTQLRYLNLSSTSLRKINAAWFKNM PHLKVLDLEFNYLVGEIVSGAFLTMLPRLEILDLSFNYIKGSYPQHINISRNFSKLLSLRAL ${\tt HLRGYVFQELREDDFQPLMQLPNLSTINLGINFIKQIDFKLFQNFSNLEIIYLSENRISPLV}$ KDTRQSYANSSSFQRHIRKRRSTDFEFDPHSNFYHFTRPLIKPQCAAYGKALDLSLNSIFFI GPNQFENLPDIACLNLSANSNAQVLSGTEFSAIPHVKYLDLTNNRLDFDNASALTELSDLEV LDLSYNSHYFRIAGVTHHLEFIQNFTNLKVLNLSHNNIYTLTDKYNLESKSLVELVFSGNRL DILWNDDDNRYISIFKGLKNLTRLDLSLNRLKHIPNEAFLNLPASLTELHINDNMLKFFNWT LLQQFPRLELLDLRGNKLLFLTDSLSDFTSSLRTLLLSHNRISHLPSGFLSEVSSLKHLDLS SNLLKTINKSALETKTTTKLSMLELHGNPFECTCDIGDFRRWMDEHLNVKIPRLVDVICASP GDQRGKSIVSLELTTCVSDVTAVILFFFTFFITTMVMLAALAHHLFYWDVWFIYNVCLAKVK GYRSLSTSQTFYDAYISYDTKDASVTDWVINELRYHLEESRDKNVLLCLEERDWDPGLAIID $\verb|NLMQSINQSKKTVFVLTKKYAKSWNFKTAFYLALQRLMDENMDVIIFILLEPVLQHSQYLRL|$ RQRICKSSILQWPDNPKAEGLFWQTLRNVVLTENDSRYNNMYVDSIKQY

1



FIGURE 212

CCAGGTCCAACTGCACCTCGGTTCTATCGATTGAATTCCCCGGGGATCCTCTAGAGATCCCT CGACCTCGACCCACGCGTCCGCCAAGCTGGCCCTGCACGGCTGCAAGGGAGGCTCCTGTGGA . CAGGCCAGGCAGGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGC AAGGGCTAGGGTCCATCTCCAGTCCCAGGACACAGCAGCGGCCACCATGGCCACGCCTGGGC TCCAGCAGCATCAGCAGCCCCCAGGACCGGGGAGGCACAGGTGGCCCCCACCACCACCAGGAGGA GCAGCTCCTGCCCCTGTCCGGGGGATGACTGATTCTCCTCCGCCAGGCCACCCAGAGGAGAA GGCCACCCGCCTGGAGGCACAGGCCATGAGGGGCTCTCAGGAGGTGCTGCTGATGTGGCTT CTGGTGTTGGCAGTGGGCGCACAGAGCACGCCTACCGGCCCGGCCGTAGGGTGTGTGCTGT CCGGGCTCACGGGGACCCTGTCTCCGAGTCGTTCGTGCAGCGTGTGTACCAGCCCTTCCTCA CCACCTGCGACGGGCACCGGGCCTGCAGCACCTACCGAACCATCTATAGGACCGCCTACCGC CGCAGCCCTGGGCTGGCCCTGCCAGGCCTCGCTACGCGTGCTGCCCCGGCTGGAAGAGGAC CAGCGGGCTTCCTGGGGCCTGTGGAGCAGCAATATGCCAGCCGCCATGCCGGAACGGAGGGA GCTGTGTCCAGCCTGGCCGCTGCCGCTGCCGGGGTGACACTTGCCAGTCA GATGTGGATGAATGCAGTGCTAGGAGGGGGGGGCTGTCCCCAGCGCTGCATCAACACCGCCGG CAGTTACTGGTGCCAGTGTTGGGAGGGGCACAGCCTGTCTGCAGACGGTACACTCTGTGTGC CCAAGGGAGGCCCCCCAGGGTGGCCCCCAACCCGACAGGAGTGGACAGTGCAATGAAGGAA GAAGTGCAGAGGCTGCAGTCCAGGGTGGACCTGCTGGAGGAGAAGCTGCAGCTGGTGCTGGC CCCACTGCACAGCCTGGCCTCGCAGGCACTGGAGCATGGGCTCCCGGACCCCGGCAGCCTCC GAGGAGCAGCTGGGGTCCTGCTCCTGCAAGAAAGACTCGTGACTGCCCAGCGCCCCAGGCTG GACTGAGCCCCTCACGCCGCCCTGCAGCCCCCATGCCCCTGCCCAACATGCTGGGGGTCCAG AAGCCACCTCGGGGTGACTGAGCGGAAGGCCAGGCAGGCCTTCCTCCTCTTCCTCCTCCCCC TTCCTCGGGAGGCTCCCCAGACCCTGGCATGGGATGGGCTGGGATCTTCTCTGTGAATCCAC CCCTGGCTACCCCACCCTGGCTACCCCAACGGCATCCCAAGGCCAGGTGGGCCCTCAGCTG AGGGAAGGTACGAGCTCCCTGCTGGAGCCTGGGACCCATGGCACAGGCCAGGCAGCCCGGAG GCTGGGTGGGGCCTCAGTGGGGGCTGCTGCCTGACCCCCAGCACAATAAAAATGAAACGTGA CGACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAAT



MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR . CPAGWRGDTCQSDVDECSARRGGCPQRCINTAGSYWCQCWEGHSLSADGTLCVPKGGPPRVA PNPTGVDSAMKEEVQRLQSRVDLLEEKLQLVLAPLHSLASQALEHGLPDPGSLLVHSFQQLG RIDSLSEQISFLEEQLGSCSCKKDS

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FIGURE 214

GCCAGGCAGGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCCTGAGGCCCCAGCAAG GGCTAGGGTCCATCTCCAGTCCCAGGACACAGCAGCGCCACCATGGCCACGCCTGGGCTCC AGCAGCATCAGAGCAGCCCCTGTGGTTGGCAGCAAAGTTCAGCTTGGCTGGGCCCGCTGTGA GGGGCTTCGCGCTACGCCCTGCGGTGTCCCGAGGGCTGAGGTCTCCTCATCTTCTCCCTAGC AAAGCCACATCTGTAGCCAGGATGAGCAGTGTGAATCCAGGCAGCCCCCAGGACCGGGGAGG CACAGGTGGCCCCCACCACCGGAGGAGCAGCTCCTGCCCCTGTCCGGGGGATGACTGATTC ${\tt TCTCAGGAGGTGCTGATGTGGCTTCTGGTGTTGGCAGTGGGCGCACAGAGCACGCCTA}^{.}$ CCGGCCCGGCCGTAGGGTGTGTGCCGGGCTCACGGGGACCCTGTCTCCGAGTCGTTCG TGCAGCGTGTGTACCAGCCTTCCTCACCACCTGCGACGGGCACCGGGCCTGCAGCACCTAC CGAACCATCTATAGGACCGCCTACCGCCGCAGCCCTGGGCTGGCCTGCCAGGCCTCGCTA CGCGTGCTGCCCCGGCTGGAAGAGGACCAGCGGCTTCCTGGGGCCTGTGGAGCAGCAATAT GCCAGCCGCCATGCCGGAACGGAGGGAGCTGTCCAGCCTGGCCGCTGCCCTGCA GGATGGCGGGGTGACACTTGCCAGTCAGATGTGGATGAATGCAGTGCTAGGAGGGGGGGCTG TCCCCAGCGCTGCATCAACACCGCCGGCAGTTACTGGTGCCAGTGTTGGGAGGGGCACAGCC TGTCTGCAGACGGTACACTCTGTGTGCCCAAGGGAGGGCCCCCAGGGTGGCCCCCAACCCG ${\tt ACAGGAGTGGACAGTGCAATGAAGGAAGAAGTGCAGGGTGGACCTGCT}$ ${\tt GGAGGAGAGCTGCAGCTGGCCCCACTGCACAGCCTGGCCTCGCAGGCACTGGAGC}$ ATGGGCTCCCGGACCCCGGCAGCCTCCTGGTGCACTCCTTCCAGCAGCTCGGCCGCATCGAC $\verb|CTCG| \frac{\textbf{TGA}}{\textbf{CTGCCCAGCCTCCAGGCTGGACTGAGCCCCTCACGCCCCTGCAGCCCCCATG}|$ CCCCTGCCCAACATGCTGGGGGTCCAGAAGCCACCTCGGGGTGACTGAGCGGAAGGCCAGGC AGGGCCTTCCTCCTCCTCCCCTTCCTCGGGAGGCTCCCCAGACCCTGGCATGGGAT GGGCTGGGATCTTCTCTGTGAATCCACCCCTGGCTACCCCCACCCTGGCTACCCCAACGGCA ${\tt TCCCAAGGCCAGGTGGACCCTCAGCTGAGGGAAGGTACGAGCTCCCTGCTGGAGCCTGGGAC}$ CCATGGCACAGGCCAGGCCCGGAGGCTGGGTGGGGCCTCAGTGGGGGGCTGCTGAC CCCCAGCACAATAAAAATGAAACGTG



MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR CPAGWRGDTCQSDVDECSARRGGCPQRCINTAGSYWCQCWEGHSLSADGTLCVPKGGPPRVA PNPTGVDSAMKEEVQRLQSRVDLLEEKLQLVLAPLHSLASQALEHGLPDPGSLLVHSFQQLG RIDSLSEQISFLEEQLGSCSCKKDS

CCCACGCGTCCGAAGCTGGCCCTGCACGGCTGCAAGGGAGGCTCCTGTGGACAGGCCAGGCA GGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGCAAGGGCTAGGG TCCATCTCCAGTCCCAGGACACAGCAGCGCCACCATGGCCACGCCTGGGCTCCAGCAGCAT CAGCAGCCCCAGGACCGGGGGGGCACCAGGTGGCCCCCACCACCCGGAGGAGCAGCTCCTGC CCCTGTCCGGGGGATGACTGATTCTCCTCCGCCAGGCCACCCAGAGGAGAAGGCCACCCCGC ${\tt CTGGAGGCACAGGCC} \underline{{\tt ATG}} {\tt AGGGGGCTCTCAGGAGGTGCTGCTGATGTGGCTTCTGGTGTTGGCC}$ AGTGGGCGGCACAGAGCACGCCTACCGGCCCGGCCGTAGGGTGTGTGCTGTCCGGGCTCACG GGGACCCTGTCTCCGAGTCGTTCGTGCAGCGTGTGTACCAGCCCTTCCTCACCACCTGCGAC GGGCACCGGGCCTGCAGCACCTACCGAACCATCTATAGGACCGCCTACCGCCGCAGCCCTGG GCTGGCCCTGCCAGGCCTCGCTACGCGTGCTGCCCCGGCTGGAAGAGACCAGCGGGCTTC CCTGGCCGCTGCCCTGCAGGATGGCGGGGTGACACTTGCCAGTCAGATGTGGATGA ATGCAGTGCTAGGAGGGGGGGCTGTCCCCAGCGCTGCGTCAACACCGCCGGCAGTTACTGGT GCTGCAGTCCAGGGTGGACCTGCTGGAGGAGAAGCTGCAGCTGGTGCTGGCCCCACTGCACA GCCTGGCCTCGCAGGCACTGGAGCATGGGCTCCCGGACCCCGGCAGCCTCCTGGTGCACTCC ${\tt GGGGTCCTGCTGCAAGAAGACTCG}{\tt TGA}{\tt CTGCCCAGCGCCCCAGGCTGGACTGAGCCCC}$ TCACGCCGCCCTGCAGCCCCATGCCCCTGCCCAACATGCTGGGGGTCCAGAAGCCACCTCG GGGTGACTGAGCGGAAGGCCAGGCAGGCCTTCCTCCTCTCCTCCCCCTTCCTCGGGAG GCTCCCCAGACCCTGGCATGGGATGGGCTGGGATCTTCTCTGTGAATCCACCCCTGGCTACC CCCACCCTGGCTACCCCAACGGCATCCCAAGGCCAGGTGGGCCCTCAGCTGAGGGAAGGTAC CCTCAGTGGGGGCTGCTGCCTGACCCCCAGCACAATAAAAATGAAACGTG

MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR CPAGWRGDTCQSDVDECSARRGGCPQRCVNTAGSYWCQCWEGHSLSADGTLCVPKGGPPRVA PNPTGVDSAMKEEVQRLQSRVDLLEEKLQLVLAPLHSLASQALEHGLPDPGSLLVHSFQQLG RIDSLSEQISFLEEQLGSCSCKKDS

GGTTGCCACAGCTGGTTTAGGGCCCCGACCACTGGGGCCCCTTGTCAGGAGGAGACAGCCTC CCGGCCCGGGGAGGACAAGTCGCTGCCACCTTTGGCTGCCGACGTGATTCCCTGGGACGGTC CGTTTCCTGCCGTCAGCTGCCGGCCGAGTTGGGTCTCCGTGTTTCAGGCCGGCTCCCCCTTC CTGGTCTCCCCTTCTCCCGCTGGGCCGGTTTATCGGGAGGAGATTGTCTTCCAGGGCTAGCAA TTGGACTTTTGATGATGTTTGACCCAGCGGCAGGAATAGCAGGCAACGTGATTTCAAAGCTG GGCTCAGCCTCTGTTTCTCTCTCGTGTAATCGCAAAACCCATTTTGGAGCAGGAATTCCAA AACACCTTTTGCTGTGATGGCCGCGTCATGATGGCCCGGCAAAAGGGCCATTTTCTACCTGAC CCTTTTCCTCATCCTGGGGACATGTACACTCTTCTTCGCCTTTGAGTGCCGCTACCTGGCTG TTCAGCTGTCTCCTGCCATCCCTGTATTTGCTGCCATGCTCTTCCTTTTCTCCATGGCTACA CTGTTGAGGACCAGCTTCAGTGACCCTGGAGTGATTCCTCGGGCGCTACCAGATGAAGCAGC TTTCATAGAAATGGAGATAGAAGCTACCAATGGTGCGGTGCCCCAGGGCCAGCGACCACCGC CTCGTATCAAGAATTTCCAGATAAACAACCAGATTGTGAAACTGAAATACTGTTACACATGC AAGATCTTCCGGCCTCCCGGGCCTCCCATTGCAGCATCTGTGACAACTGTGTGGAGCGCTT CGACCATCACTGCCCCTGGGTGGGGAATTGTGTTGGAAAGAGGAACTACCGCTACTTCTACC TCTTCATCCTTTCTCTCTCCCTCCTCACAATCTATGTCTTCGCCTTCAACATCGTCTATGTG TCCTCGTGGCTCTCAACCAGACAACCAATGAAGACATCAAAGGATCATGGACAGGGAAGAAT CGCGTCCAGAATCCCTACAGCCATGGCAATATTGTGAAGAACTGCTGTGAAGTGCTGTGTGG CCCCTTGCCCCCAGTGTGCTGGATCGAAGGGGTATTTTGCCACTGGAGGAAAGTGGAAGTC GACCTCCCAGTACTCAAGAGACCAGTAGCAGCCTCTTGCCACAGAGCCCAGCCCCCACAGAA CACCTGAACTCAAATGAGATGCCGGAGGACAGCAGCACTCCCGAAGAGATGCCACCTCCAGA GCCCCAGAGCCACACAGGAGGCAGCTGAAGCTGAGAAG<mark>TAG</mark>CCTATCTATGGAAGAGACT TTTGTTTGTGTTTAATTAGGGCTATGAGAGATTTCAGGTGAGAAGTTAAACCTGAGACAGAG AGCAAGTAAGCTGTCCCTTTTAACTGTTTTTCTTTGGTCTTTAGTCACCCAGTTGCACACTG GCATTTTCTTGCTGCAAGCTTTTTTAAATTTCTGAACTCAAGGCAGTGGCAGAAGATGTCAG TCACCTCTGATAACTGGAAAAATGGGTCTCTTGGGCCCTGGCACTGGTTCTCCATGGCCTCA GCCACAGGGTCCCCTTGGACCCCCTCTCTTCCCTCCAGATCCCAGCCCTCCTGCTTGGGGTC ACTGGTCTCATTCTGGGGCTAAAAGTTTTTGAGACTGGCTCAAATCCTCCCAAGCTGCTGCA CGTGCTGAGTCCAGAGGCAGTCACAGAGACCTCTGGCCAGGGGATCCTAACTGGGTTCTTGG GGTCTTCAGGACTGAAGAGGAGGGAGAGTGGGGTCAGAAGATTCTCCTGGCCACCAAGTGCC AGCATTGCCCACAAATCCTTTTAGGAATGGGACAGGTACCTTCCACTTGTTGTANNNNNNN NNNNNNNNNNNNNNNNNTTGTTTTTCCTTTTGACTCCTGCTCCCATTAGGAGCAGGAATG GCAGTAATAAAAGTCTGCACTTTGGTCATTTCTTTTCCTCAGAGGAAGCCCGAGTGCTCACT TAAACACTATCCCCTCAGACTCCCTGTGTGAGGCCTGCAGAGGCCCTGAATGCACAAATGGG CCCTCTCGGGTAACTCACCCTAAGGCCTCGGCCCACCTCTGGCTATGGTAACCACACTGGGG GCTTCCTCCAAGCCCCGCTCTTCCAGCACTTCCACCGGCAGAGTCCCAGAGCCACTTCACCC TGGGGGTGGGCTGTGGCCCCAGTCAGCTCTGCTCAGGACCTGCTCTATTTCAGGGAAGAAG ATTTATGTATTATATGTGGCTATATTTCCTAGAGCACCTGTGTTTTCCTCTTTCTAAGCCAG GGTCCTGTCTGGATGACTTATGCGGTGGGGGGGTGTAAACCGGAACTTTTCATCTATTTGAA GGCGATTAAACTGTGTCTAATGCA

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MSVMVVRKKVTRKWEKLPGRNTFCCDGRVMMARQKGIFYLTLFLILGTCTLFFAFECRYLAV.
QLSPAIPVFAAMLFLFSMATLLRTSFSDPGVIPRALPDEAAFIEMEIEATNGAVPQGQRPPP
RIKNFQINNQIVKLKYCYTCKIFRPPRASHCSICDNCVERFDHHCPWVGNCVGKRNYRYFYL
FILSLSLLTIYVFAFNIVYVALKSLKIGFLETLKETPGTVLEVLICFFTLWSVVGLTGFHTF
LVALNQTTNEDIKGSWTGKNRVQNPYSHGNIVKNCCEVLCGPLPPSVLDRRGILPLEESGSR
PPSTQETSSSLLPQSPAPTEHLNSNEMPEDSSTPEEMPPPEPPPQEAAEAEK

AAAACCCTGTATTTTTTACAATGCAAATAGACAATNANCCTGGAGGTCTTTGAATTAGGTAT
TATAGGGATGGTGGGGTTGATTTTTNTTCCTGGAGGCTTTTGGCTTTTGGACTCTCNCTTTCT
CCCACAGAGCNCTTCGACCATCACTGCCCCTGGGTGGGGAATTGTGTTGGAAAGAGGAACTA
CCGCTANTTCTACCTCTTCATCCTTTNTCTCTCCCNCCTCACAATCTATGTCTTCGCCTTCA
ACATCGT

٩,



FIGURE 221

GTTGTGTCCTTCAGCAAAACAGTGGATTTAAATCTCCTTGCACAAGCTTGAGAGCAACACAA TCTATCAGGAAAGAAAGAAAAAACCGAACCTGACAAAAAAGAAGAAAAAGAAGAAGAAGA AAAAAAATCATCAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCAC GGGGCTGGCTCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCC CCAAAGCTATGGACAACGTGACGGTCCGGCAGGGGGGAGAGCGCCACCCTCAGGTGCACTATT GACAACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGA CAAGTGGTGCCTGGATCCTCGCGTGGTCCTTCTGAGCAACACCCAAACGCAGTACAGCATCG CACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAAATTGTAGAGATTTC TTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACTGGTAGAC GAATACTTGGAAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAGTGCAGTGCCTC CAATGACGTGGCCGCGCGCGTGGTACGGAGGTAAAGGTCACCGTGAACTATCCACCATACA TTTCAGAAGCCAAGGGTACAGGTGTCCCCGTGGGACAAAAGGGGACACTGCAGTGTGAAGCC TCAGCAGTCCCCTCAGCAGAATTCCAGTGGTACAAGGATGACAAAAGACTGATTGAAGGAAA GAAAGGGGTGAAAGTGGAAAACAGACCTTTCCTCTCAAAACTCATCTTCTAATGTCTCTG AACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAGCTGGGCCACACCAATGCCAGC ATCATGCTATTTGGTCCAGGCGCCGTCAGCGAGGTGAGCAACGGCACGTCGAGGAGGGCAGG $\tt CTGCGTCTGGCTGCTCTTCTGGTCTTGCACCTGCTTCTCAAATTT{\color{red}{\textbf{TGA}}} \tt TGTGAGTGCC$ CGACAGCAACCAATCAGATATATACAAATGAAATTAGAAGAAACACAGCCTCATGGGACAGA AATTTGAGGGAGGGAACAAAGAATACTTTGGGGGGAAAAGAGTTTTAAAAAAAGAAATTGAA AATTGCCTTGCAGATATTTAGGTACAATGGAGTTTTCTTTTCCCAAACGGGAAGAACACAGC ACACCCGGCTTGGACCCACTGCAAGCTGCATCGTGCAACCTCTTTGGTGCCAGTGTGGGCAA GGGCTCAGCCTCTCTGCCCACAGAGTGCCCCCACGTGGAACATTCTGGAGCTGGCCATCCCA AATTCAATCAGTCCATAGAGACGAACAGAATGAGACCTTCCGGCCCAAGCGTGGCGCTGCGG GCACTTTGGTAGACTGTGCCACCACGGCGTGTGTTGTGAAACGTGAAATAAAAAGAGCAAAA AAAAA

MKTIQPKMHNSISWAIFTGLAALCLFQGVPVRSGDATFPKAMDNVTVRQGESATLRCTIDNR VTRVAWLNRSTILYAGNDKWCLDPRVVLLSNTQTQYSIEIQNVDVYDEGPYTCSVQTDNHPK TSRVHLIVQVSPKIVEISSDISINEGNNISLTCIATGRPEPTVTWRHISPKAVGFVSEDEYL EIQGITREQSGDYECSASNDVAAPVVRRVKVTVNYPPYISEAKGTGVPVGQKGTLQCEASAV PSAEFQWYKDDKRLIEGKKGVKVENRPFLSKLIFFNVSEHDYGNYTCVASNKLGHTNASIML FGPGAVSEVSNGTSRRAGCVWLLPLLVLHLLKF





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FIGURE 224

ATGGCTGGTGACGGCGGGCCGGGCCAGGGGCCGGGCCCGGGAGCGGCCAGCTG CCGGGAGCCCTGAATCACCGCCTGGCCCGACTCCACC<u>ATG</u>AACGTCGCGCTGCAGGAGCTGG CTGGAGCTGGTCTTAGCAGGTGCCTCTCTACTGCTGCTGCACTGCTTCTGGGCTGCCTTGT GGCCCTAGGGGTCCAGTACCACAGAGACCCATCCCACAGCACCTGCCTTACAGAGGCCTGCA TTCGAGTGGCTGGAAAAATCCTGGAGTCCCTGGACCGAGGGGTGAGCCCCTGTGAGGACTTT TACCAGTTCTCCTGTGGGGGCTGGATTCGGAGGAACCCCCTGCCCGATGGGCGTTCTCGCTG GAACACCTTCAACAGCCTCTGGGACCAAAACCAGGCCATACTGAAGCACCTGCTTGAAAACA CCACCTTCAACTCCAGCAGTGAAGCTGAGCAGAAGACACAGCGCTTCTACCTATCTTGCCTA CAGGTGGAGCGCATTGAGGAGCTGGGAGCCCAGCCACTGAGAGACCTCATTGAGAAGATTGG TGGTTGGAACATTACGGGGCCCTGGGACCAGGACAACTTTATGGAGGTGTTGAAGGCAGTAG CAGGGACCTACAGGGCCACCCCATTCTTCACCGTCTACATCAGTGCCGACTCTAAGAGTTCC AACAGCAATGTTATCCAGGTGGACCAGTCTGGGCTCTTTCTGCCCTCTCGGGATTACTACTT AAACAGAACTGCCAATGAGAAAGTGCTCACTGCCTATCTGGATTACATGGAGGAACTGGGGA TGCTGCTGGGTGGGCGCCCACCTCCACGAGGGAGCAGATGCAGCAGGTGCTGGAGTTGGAG ATACAGCTGGCCAACATCACAGTGCCCCAGGACCAGCGGCGCGACGAGGAGAAGATCTACCA CAAGATGAGCATTTCGGAGCTGCAGGCTCTGGCGCCCTCCATGGACTGGCTTGAGTTCCTGT TATTTGCAGCAGGTGTCAGAGCTCATCAACCGCACGGAACCAAGCATCCTGAACAATTACCT GATCTGGAACCTGGTGCAAAAGACAACCTCAAGCCTGGACCGACGCTTTGAGTCTGCACAAG AGAAGCTGCTGGAGACCCTCTATGGCACTAAGAAGTCCTGTGTGCCGAGGTGGCAGACCTGC ATCTCCAACACGGATGACGCCCTTGGCTTTGCTTTGGGGTCACTCTTCGTGAAGGCCACGTT TGACCGGCAAAGCAAAGAAATTGCAGAGGGGATGATCAGCGAAATCCGGACCGCATTTGAGG AGGCCCTGGGACAGCTGGTTTGGATGGATGAGAAGACCCGCCAGGCAGCCAAGGAGAAAGCA GATGCCATCTATGATATGATTGGTTTCCCAGACTTTATCCTGGAGCCCAAAGAGCTGGATGA TGTTTATGACGGGTACGAAATTTCTGAAGATTCTTTCTTCCAAAACATGTTGAATTTGTACA ACTTCTCTGCCAAGGTTATGGCTGACCAGCTCCGCAAGCCTCCCAGCCGAGACCAGTGGAGC ATGACCCCCAGACAGTGAATGCCTACTACCTTCCAACTAAGAATGAGATCGTCTTCCCCGC TGGCATCCTGCAGGCCCCCTTCTATGCCCGCAACCACCCCAAGGCCCTGAACTTCGGTGGCA TCGGTGTGGTCATGGGCCATGAGTTGACGCATGCCTTTGATGACCAAGGGCGCGAGTATGAC AAAGAAGGGAACCTGCGGCCCTGGTGGCAGATGAGTCCCTGGCAGCCTTCCGGAACCACAC GGCCTGCATGGAGGAACAGTACAATCAATACCAGGTCAATGGGGAGAGGCTCAACGGCCGCC AGACGCTGGGGGAGAACATTACTGACAACGGGGGGGCTGAAGGCTGCCTACAATGCTTACAAA GCTCTTCTTCGTGGGATTTGCCCAGGTGTGGTGCTCGGTCCGCACACCAGAGAGCTCTCACG AGGGGCTGGTGACCGACCCCCACAGCCCTGCCCGCTTCCGCGTGCTGGGCACTCTCCCAAC TCCCGTGACTTCCTGCGGCACTTCGGCTGCCCTGTCGGCTCCCCCATGAACCCAGGGCAGCT ${ t GTGTGAGGTGTGG}$ GCTCTCCTGACAAAGCTGTTTGCTCTTGGGTTGGGAGGAAGCAAATGCAAGCTGGGCTGGGT CTAGTCCCTCCCCCCACAGGTGACATGAGTACAGACCCTCCTCAATCACCACATTGTGCCT CTGCTTTGGGGGTGCCCCTGCCTCCAGCAGAGCCCCCACCATTCACTGTGACATCTTTCCGT



MNVALQELGAGSNVGFQKGTRQLLGSRTQLELVLAGASLLLAALLLGCLVALGVQYHRDPSH STCLTEACIRVAGKILESLDRGVSPCEDFYQFSCGGWIRRNPLPDGRSRWNTFNSLWDQNQA ILKHLLENTTFNSSSEAEQKTQRFYLSCLQVERIEELGAQPLRDLIEKIGGWNITGPWDQDN FMEVLKAVAGTYRATPFFTVYISADSKSSNSNVIQVDQSGLFLPSRDYYLNRTANEKVLTAY LDYMEELGMLLGGRPTSTREQMQQVLELEIQLANITVPQDQRRDEEKIYHKMSISELQALAP SMDWLEFLSFLLSPLELSDSEPVVVYGMDYLQQVSELINRTEPSILNNYLIWNLVQKTTSSL DRRFESAQEKLLETLYGTKKSCVPRWQTCISNTDDALGFALGSLFVKATFDRQSKEIAEGMI SEIRTAFEEALGQLVWMDEKTRQAAKEKADAIYDMIGFPDFILEPKELDDVYDGYEISEDSF FQNMLNLYNFSAKVMADQLRKPPSRDQWSMTPQTVNAYYLPTKNEIVFPAGILQAPFYARNH PKALNFGGIGVVMGHELTHAFDDQGREYDKEGNLRPWWQNESLAAFRNHTACMEEQYNQYQV NGERLNGRQTLGENITDNGGLKAAYNAYKAWLRKHGEEQQLPAVGLTNHQLFFVGFAQVWCS VRTPESSHEGLVTDPHSPARFRVLGTLSNSRDFLRHFGCPVGSPMNPGQLCEVW



FIGURE 226A

GGCAGCGGCCTCCAGCCAAGCCCGTCCCCGCAGGCTGCACCTTCGGCGGGAAGGTCTATGCC TTGGACGAGACGTGGCACCCGGACCTAGGGGAGCCATTCGGGGTGATGCGCTGCGTGCTGTG CGCCTGCGAGGCGCAGTGGGGTCGCCGTACCAGGGGCCCTGGCAGGGTCAGCTGCAAGAACA TCAAACCAGAGTGCCCAACCCCGGCCTGTGGGCAGCCGCGCCAGCTGCCGGGACACTGCTGC CAGACCTGCCCCAGGACTTCGTGGCGCTGCTGACAGGGCCGAGGTCGCAGGCGGTGGCACG AGCCCGAGTCTCGCTGCGCTCTAGCCTCCGCTTCTCTATCTCCTACAGGCGGCTGGACC GCCCTACCAGGATCCGCTTCTCAGACTCCAATGGCAGTGTCCTGTTTGAGCACCCTGCAGCC CCCACCCAAGATGGCCTGGTCTGTGGGGGTGTGGCGGCAGTGCCTCGGTTGTCTCTGCGGCT CCTTAGGGCAGAACAGCTGCATGTGGCACTTGTGACACTCACCCTTCAGGGGAGGTCT GGGGGCCTCTCATCCGGCACCGGGCCCTGTCCCCAGAGACCTTCAGTGCCATCCTGACTCTA GAAGGCCCCCACCAGCAGGGCGTAGGGGGCATCACCCTGCTCACTCTCAGTGACACAGAGGA CTCCTTGCATTTTTTGCTGCTCTTCCGAGGCCTTGCAGGACTAACCCAGGTTCCCTTGAGGC TCCAGATTCTACACCAGGGGCAGCTACTGCGAGAACTTCAGGCCAATGTCTCAGCCCAGGAA GGAGCTGCAGATGGCCCTGGAGTGGGCAGGCAGGGCTGCGCATCAGTGGACACATTG CTGCCAGGAAGAGCTGCGACGTCCTGCAAAGTGTCCTTTGTGGGGCTAATGCCCTGATCCCA GTCCAAACGGGTGCTGCCGGCTCAGCCAGCCTCACTCTGCTAGGAAATGGCNCCCTGATCCT CCAGGTGCAATTGGTAGGGACAACCAGTGAGGTGGTGGCCATGACACTGGAAACCAAGCCTC CCGTGGGTATCTGCCCTGGGCTGGGGTGCCCGAGGGGCTCATATGCTGCTGCAGAATGAGCT CTTCCTGAACGTGGGCACCAAGGACTTCCCAGACGGAGAGCTTCGGGGGCAACGTGGCTGCC CTGCCCTACTGTGGGGCATAGCGCCCGCCCTGCCCGTGCCCCTAGCAGGAGCCCTGGTGCTA CCCCCTGTGAAGAGCCAAGCAGCAGGGCACGCCTGGCTTTCCTTGGATACCCACTGTCACCT GCACTATGAAGTGCTGCTGGCTGGGCTTGGTGGCTCAGAACAAGGCACTGTCACTGCCCACC TCCTTGGGCCTCCTGGAACGCCAGGGCCTCGGCGGCTGCTGAAGGGATTCTATGGCTCAGAG GCCCAGGGTGTGAAGGACCTGGAGCCGGAACTGCTGCGGCACCTGGCAAAAGGCATGGC TTCCCTGATGATCACCACCAAGGTAGCCCCAGAGGGGAGCTCCGAGGGCAGCCTCTCCCC AGGTGCACATAGCCAACCAATGTGAGGTTGGCGGACTGCGCCTGGAGGCGGCCGGGCCGAG GGGGTGCGGGCGCTGGGGGCTCCGGATACAGCCTCTGCTGCGCCGCCTGTGGTGCCTGGTCT CCCGGCCCTAGCGCCCCAAACCTGGTGGTCCTGGGCGCCCCGAGACCCCAACACATGCT TCTTCGAGGGGCAGCAGCGCCCCACGGGGCTCGCTGGGCCCCAACTACGACCCGCTCTGC TCACTCTGCACCTGCCAGAGACGAACGGTGATCTGTGACCCGGTGGTGTGCCCACCGCCCAG CTGCCCACACCCGGTGCAGGCTCCCGACCAGTGCTGCTGTTTGCCCTGGCTGCTATTTTG TTAATTAAGTGTGCTGTCTGCACCTGCAAGCAGGGGGGCACTGGAGAGGTGCACTGTGAGAA GGTGCAGTGTCCCCGGCTGGCCTGTGCCCAGCCTGTGCGTGTCAACCCCACCGACTGCTGCA AACAGTGTCCAGGTGAGGCCCACCCCCAGCTGGGGGACCCCATGCAGGCTGATGGGCCCCGG GGCTGCCGTTTTGCTGGGCAGTGGTTCCCAGAGAGTCAGAGCTGGCACCCCTCAGTGCCCCC GTTTGGAGAGATGAGCTGTATCACCTGCAGATGTGGGGTAAGTGGGGAGCAGAGGCTTGTGT GAGGTGGGTACTGGGAGCCTGGTCTGGAGTAGGGAGACCTTCCCAGGGAGGTCCCTGAAGAA AGGCAGGGGTGCCTCACTGTGAGCGGGATGACTGTTCACTGCCACTGTCCTGTGGCTCGGGG AAGGAGAGTCGATGCTGTTCCCGCTGCACGGCCCACCGGCGGCGTAAGTGAGGGAGTCCAGG GTCAGCAGCTGTGAGTGGAGGGCTCACCTGCCTGTGGGACTCCTGATCAGGGAAGGGAGCAC TCACTGTGTGCAGGAACAGTGCAGCCTGCCTCACAAGTGCCATTCCAATCCACCCTCACAGC AACCTGGTGGAATTGTTATTTATGACCTTTTCTTTACAAATGAGATTTCTGAAGCTCAGAGA **AATTAAGCAACGAGATGAAGGTCACCCAGCTGTGTGCACCTGTTTTAGAAAATACTGGC**





FIGURE 226B

CTTTCTGGGACCAAGGCAGGGATGCTTTGCCCTGCCCTCTATGCCTCTCTGTGCCTCTCCAC TCCCTCTCCCTCCAACATTCCCTCCCTTCTGTCTCCAGCAGCCCCAGAGACCAGAACT AGAGGATGGGGCCTGAGCTGGGGAAGGGGTGGCATCGAGGACCTTCTTGCATTCTCCTGTGG GAAGCCCAGTGCCTTTGCTCCTGTCCTGCCTCTACTCCCACCCCACTACCTCTGGGAAC CACAGCTCCACAAGGGGGAGAGGCAGCTGGGCCAGACCGAGGTCACAGCCACTCCAAGTCCT GCCCTGCCACCCTCGGCCTCTGTCCTGGAAGCCCCACCCCTTTCTTCCTGTACATAATGTCA CTGGCTTGTTGGGATTTTTAATTTATCTTCACTCAGCACCAAGGGCCCCGGACACTCCACTC TTTTCAGTCTTTGGGCATGAGGTTGGCTCTTTGTGGCCAGGAACCTGAGTGGGGCCTGGTGG AGAAGGGCCNGAGAGTAGGAGGTGAGAGAGAGGAGCTCTGACACTTGGGGAGCTGAAAGAGA CCTGGAGAGGCAGAGGATAGCGTGGCNNTTGGCTGGCATNCCTGGGTTCCGCAGAGGGGCTG GGGATGGTTCTTGAGATGGTCTAGAGACTCAAGAATTTAGGGAAGTAGAAGCAGGATTTTGA CTCAAGTTTAGTTTCCCACATCGCTGGCCTGTTTGCTGACTTCATGTTTGAAGTTGCTCCAG CCTCCCTCCCTCCCTCCCTCC



GGCCGAGCGGGGGTGCTGCCGGGCGGCCGTGATGGCTGACGGCGGGGCCGGGCAGGGGA CCGGGGCCGGGCCCGGGAGCCCGGGCCGGCCTGCCCGAC TCCACCATGAACGTCGCGCTGCAGGAGCTGGGAGCTGGCAACGTGGGATTCCAGAAGGG GACAAGACAGCTGTTAGGCTCACGCACGCAGCTGGAGCTGGTCTTAGCAGGTGCCTCTCTAC TGCTGGCTGCACTGCTTCTGGGCCTTGTGGCCCTAGGGGTCCAGTACCACAGAGACCCA TCCCACAGCACCTGCCTTACAGAGGCCTGCATTCGAGTGGCTGGAAAAATCCTGGAGTCCCT GGACCGAGGGGTGAGCCCCTGTGAGGACTTTTACCAGTTCTCCTGTGGGGGCTGGATTCGGA GGAACCCCCTGCCCGATGGGCGTTCTCGCTGGAACACCTTCAACAGCCTCTGGGACCAAAAC CAGGCCATACTGAAGCACCTGCTTGAAAACACCACCTTCAACTCCAGCAGTGAAGCTGAGCA GAAGACACAGCGCTTCTACCTATCTTGCCTACAGGTGGAGCGCATTGAGGAGCTGGGAGCCC AGCCACTGAGAGACCTCATTGAGAAGATTGGTGGTTGGAACATTACGGGGCCCTGGGACCAG GACAACTTTATGGAGGTGTTGAAGGCAGTAGCAGGGACCTACAGGGCCACCCCATTCTTCAC CGTCTACATCAGTGCCGACTCTAAGAGTTCCAACAGCAATGTTATCCAGGTGGACCAGTCTG GGCTCTTTCTGCCCTCTCGGGATTACTACTTAAACAGAACTGCCAATGAGAAAGTAAGGAAC ATCTTCCGAACCCCCATCCCTACCCCTGGCTGAGCTGGGCTGATCCCTGTTGACTTTTCCCT TTGCCAAGGGTCAGAGCAGGGAAGGTGAGCCTATCCTGTCACCTAGTGAACAAACTGCCCCT CCTTTCTTTCTTCTTCCTCCCTCCCTTCCTTCCTTCCTTCCTTCCTTCCTTCC TCTTATTCTTCTAGTAGGTTTCATAGACACCTACTGTGTGCCAGGTCCAGTGGGGGAATTCG GAGATATAAGTTTCCGAGCCATTGCCACAGGAAGCGTTCAGTGTCGATGGGTTCATGGACCT AGATAGGCTGATAACAAAGCTCACAAGAGGGTCCTGAGGATTCAGGAGAGACTTATGGAGCC AGCAAAGTCTTCCTGAAGAGATTGCATTTGAGCCAGGTCCTGTAG



ATGCCTACTACCTTCCAACTAAGAATGAGATCGTCTTCCCCGCTGGCATCCTGCAGGCCCCC TTCTATGCCCGCAACCACCCCAAGGCCCTGAACTTCGGTGGCATCGGTGTGGTCATGGGCCA TGAGTTGACGCATGCCTTTGATGACCAAGGGCGCGAGTATGACAAAGAAGGGAACCTGCGGC CCTGGTGGCAGAATGAGTCCCTGGCAGCCTTCCGGAACCACACGGCCTGCATGGAGGAACAG TACAATCAATACCAGGTCAATGGGGAGAGGCTCAACGGCCGCCAGACGCTGGGGGAGAACAT TGCTGACAACGGGGGGCTGAAGGCTGCCTACAATGCTTACAAAGCATGGCTGAGAAAGCATG GGGAGGAGCAGCTGCCAGCCGTGGGGCTCACCAACCACCAGCTCTTCTTCGTGGGATTT CCACAGCCCTGCCGCTTCCGCGTGCTGGGCACTCTCTCCAACTCCCGTGACTTCCTGCGGC ACTTCGGCTGCCCTGTCGGCTCCCCCATGAACCCAGGGCAGCTGTGTGAGGTGTGGTAGACC TGGATCAGGGGAGAAATGGCCAGCTGTCACCAGACCTGGGGCAGCTCTCCTGACAAAGCTGT GGTGACATGAGTACAGACCCTCCTCAATCACCACATTGTGCCTCTGCTTTGGGGGTGCCCCT GTCTGGGTGGGGAGGCCAGTTCCCATAGGAAGGAGTCTGCCTCTTCTGTCCCCAGGCTCACT CAGCCTGGCGGCCATGGGGCCTGCCGTGCCCCACTGTGACCCACAGGCCTGGGTGGTG ${\tt TACCTCCTGGACTTCTCCCCAGGCTCACTCAGTGCGCACTTAGGGGTGGACTCAGCTCTGTC}$ TGGCTCACCCTCACGGGCTACCCCCACCTCACCCTGTGCTCCTTGTGCCACTGCTCCCAGTG CTGCTGCTGACCTTCACTGACAGCTCCTAGTGGAAGCCCAAGGGCCTCTGAAAGCCTCCTGC TGCCCACTGTTTCCCTGGGCTGAGAGGGGAAGTGCATATGTGTAGCGGGTACTGGTTCCTGT GTCTTAGGGCACAAGCCTTAGCAAATGATTGATTCTCCCTGGACAAAGCAGGAAAGCAGATA GAGCAGGGAAAAGGAAGAACAGAGTTTATTTTTACAGAAAAGAGGGTGGGAGGGTGTGGTCT TGGCCCTTATAGGACC